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FROM THE PREFACE

The subject of surgery has now become so extensive that any work attempting to deal with it in an exhaustive manner must necessarily be so large and unwieldly as to be suitable only for purposes of reference. In any text-book of convenient size the information given must therefore be considerably condensed, and, as the first essential for the beginner is to have the fullest knowledge of the nature and characters of the diseases that he has to study, special stress is usually laid upon pathology, symptomatology and diagnosis. For the practitioner, on the other hand, who is already acquainted with these points, the great essential is full and detailed information as to the best methods of treatment. Nothing can, of course, replace experience, but it is often of the greatest advantage to have a detailed record of that of others upon which to base one's work. It is this want that the present work is intended to supply.

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THE

AMERICAN JOURNAL

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JANUARY, 1912

ORIGINAL ARTICLES

THE CAUSES OF ASCITES: A STUDY OF FIVE THOUSAND CASES.

By Richard C. Cabot, M.D.,

ASSISTANT PROFESSOR OF CLINICAL MEDICINE IN THE HARVARD MEDICAL SCHOOL, BOSTON.

I recently made a series of wrong diagnoses in cases of ascites. These failures, which were shared by some of the best diagnosticians in the country, suggested to me a study of the causes of this symptom. Until recently I had supposed that the diagnosis of the causes of ascites was one of the easiest in medicine. I was amazed to hear Dr. H. D. Rolleston say, in 1909, that he considered the diagnosis of cirrhosis a very difficult one; but in the light of recent events I have come to agree with him. To minimize the number of future mistakes, I have in this paper endeavored:

1. To tabulate from the autopsy records of the Massachusetts General Hospital the actual causes of ascites as found post mortem in 2217 autopsies (see Table I).

2. To tabulate the clinical diagnoses of ascites made at this hospital in the last forty years. Some of these diagnoses have been verified by operation or autopsy. A larger number rest on clinical evidence alone, but in most of the more dubious and more interesting cases we have operative or postmortem knowledge of the actual condition.

3. To tabulate the *rates* at which ascites accumulates in different diseases. Possibly these latter facts may be of some assistance in identifying through its more or less characteristic *tempo* of accumulation the ascites of tuberculous peritonitis.

4. To relate some of my failures and discuss the possibilities of better success in the future.

TABLE I.—Causes of Ascites as Found Post Mortem in 2217 Autopsies.

1. Cardiac weakness (due to valvular or parietal disease)	89		
2. Neoplasmic peritonitis	28		
Neoplasm of liver and glands	5	16	44
Neoplasm of stomach and glands	3		
Neoplasm of pancreas and glands	3		
Neoplasm of adrenal and glands	1		
Neoplasm of duodenum and glands	1		
Neoplasm of gut and glands	1		
Neoplasm of liver and omentum	1		
Hepatic lymphosarcoma	1		
3. Renal disease	26		
4. Cirrhosis of the liver	23		
5. Tuberculous peritonitis	10	15	
Tuberculous adenitis (tabes mesenterica)	5		
6. Adherent pericardium	9		
7. Eclampsia	3		
8. Thrombosis of the cava	1	3	
Thrombosis of the portal	1		
Thrombosis of the mesenteric	1		
9. Chronic fibrous peritonitis	3		
10. Uterine fibromyoma	3		
11. Intestinal obstruction	2		
12. Pancreatitis	1		
13. Ovarian cyst	1		
14. Acute yellow atrophy of the liver	1		
15. Status lymphaticus	1		
	224		

Table I shows the causes of fluid as found in the peritoneum in 2217 cases *at autopsy*. A quart or more of fluid was present in all these cases. Cases of septic peritonitis and hemoperitoneum are omitted. The bulk of the remaining cases are due, as was anticipated, to one of five causes: *Cardiac weakness, nephritis, abdominal neoplasms, cirrhotic liver and tuberculous peritonitis.*

I am uncertain whether the cases of adherent pericardium (all of which were associated with extensive peritoneal thickening) should be classed with the cases of cardiac weakness, or with those of chronic peritonitis. Of the other items in the list, the one most surprising to me is puerperal eclampsia.

CLINICAL STATISTICS OF ASCITES.

In some of the cases arranged in Table II the diagnosis was verified by operation or autopsy. This was the case with all the neoplasms and thromboses, and with most of the cases of intestinal obstruction and tuberculous peritonitis. But in the cardiac, renal, and hepatic cases and most of the blood diseases the evidence is wholly clinical.

Points of interest in this column are: (*a*) The frequency of ascites with ovarian cysts and tumors (see below, Table IV), and (*b*) the large figures obtained in intestinal obstruction. Probably in a considerable number of these cases the fluid may have been due to actual peritonitis associated with the obstruction.

In this table all the unstarred items represent cases actually studied in the original clinical record. The items which are starred were calculated as follows:

Throughout an eight year period I determined, by study of the clinical records, the percentage of ascitic cases among all the cases of cardiac and renal disease. These positive percentages were then applied to the total number of cases of each disease as shown by a count of the cards in the card catalogue (1870 to 1910). The starred items are, therefore, only approximately accurate.

TABLE II.—Causes of Ascites in 3086 Cases Observed Clinically at the Massachusetts General Hospital (1870–1910).

	Ascites present.	Per cent. showing ascites.	Ascites absent.	Total.
Myocardial weakness	694*	37	1183	1877
Mitral regurgitation	234*	22	1106	1340
Mitral stenosis and regurgitation	125*	24	399	524
Mitral and aortic regurgitation	72*	20	292	364
Aortic stenosis and regurgitation	87*	35	163	250
Aortic regurgitation	69*	29	169	238
Mitral stenosis	17*	8	200	217
Mitral and aortic stenosis and regurgitation	32*	42	45	77
Mitral and tricuspid regurgitation	67*	100	0	67
1. Total cases of cardiac weakness from all causes	1397*	28	3557	4954
2. Renal and cardiorenal	665*	29	1628	2293
3. Cirrhosis of the liver	325	88	42	367
4. Tuberculous peritonitis	263	82	58	321
5. Intestinal obstruction	86	43	113	199
6. Ovarian cyst, multilocular	31	7	360	391
7. Ovarian fibroma	10	50	10	20
8. Ovarian cancer	21	39	33	54
9. Ovarian sarcoma	1	20	4	5
10. Uterine fibroma	55	7	668	723
11. Neoplasmic peritonitis	53	82	11	64
12. Cancer of liver and lymphatic glands	30	20	118	148
13. Cancer of intestine and lymphatic glands	56	24	169	225
14. Cancer of pancreas and lymphatic glands	11	22	39	50
15. Malignant lymphoma (thoracic and abdominal)	5	50	5	10
16. Adherent pericardium	36	76	11	47
17. Pernicious anemia	15	7	199	214
18. Leukemia	12	13	76	88
19. Syphilis of the liver, etc.	4	40	6	10
20. Thrombosis (vena cava)	1	100	0	1
21. Thrombosis (portal)	1	100	0	1
22. Thrombosis (mesentery)	8	80	2	10
	3086		7109	10,195

Table III requires little explanation. The number of ounces of fluid between two exhaustive tappings is divided by the number of days intervening. There is a chance for error here in that the tappings, which were supposed to empty the peritoneal cavity, may, in fact, have left some fluid behind. But I do not think that this error is sufficiently serious to interfere with my results.

* Cases of ascites for the thirty-year period estimated by applying the known percentage during an eight-year period to the total number of cases.

I present herewith notes of 9 cases, illustrating some points of diagnostic interest and difficulty.

1. A case of cirrhosis without alcoholic history and with signs pointing rather to tuberculous peritonitis or cardiac dropsy.

2. A case of ovarian fibroma producing effusion in the belly and left chest; mistaken for tuberculous peritonitis.

3. A case very similar to the last, but turning out to be, in fact, tuberculous peritonitis.

4. A case of nephritis, in which the only symptom complained of was a rapidly recurrent ascites.

5. A case of fairly obvious cirrhosis; successful omentopexy.

6. A case first operated on for tuberculous peritonitis—none found. Later, cardiolysis was done for supposed pericardial cirrhosis. Slight improvement.

7. A case of supposed tuberculous peritonitis in a young girl. Tapping revealed mucilaginous fluid as from an ovarian cyst. Operation confirmed this.

8. Case of supposed splenic anemia with ascites. Prepared for operation. Evidence of syphilis found at the last moment. Disappearance of ascites and all other symptoms under Hg and KI.

9. Neoplasmic peritonitis.

CASE I.—*Ascites and edema of legs, old pleurisy with marked displacement of the heart, epithelioma of lower lid; patient not alcoholic; death after operation; autospy; cirrhosis and portal thrombosis.*

A housepainter, aged fifty-six years, who had taken alcohol only occasionally and in moderate amounts, noticed edema of his ankles seven weeks ago. A week later his belly swelled up, and he needed three tappings in six weeks, 8 or 9 quarts being withdrawn each time. Has lost 30 pounds in four months.

Examination. The right lower lid contained a small nodule showing all the characteristics of epithelioma. The heart was displaced so that its apex was in the anterior axillary line, while the right border of dulness was at the *left* sternal margin. There was a soft systolic murmur at the apex. The pulmonic second sound was not accentuated.

There was evidence of edema at the bases of the lungs. The belly contained a large amount of serous fluid, 250 ounces accumulating between two tappings sixteen days apart—an average of over 15 ounces a day. The fluids were 1006 and 1008 in gravity, and showed 80 per cent. and 90 per cent. of lymphocytes respectively in their sediments. Culture and animal inoculation negative. Fever was absent, and there was no reaction after the subcutaneous injection of 10 mg. of tuberculin.

There was some excess of neutral fat in the stools, suggesting to Dr. H. F. Hewes the stools of tuberculous peritonitis.

In diagnosis we considered cirrhosis of the liver, tuberculous peritonitis, and also the possibility that misplacement of the heart,

owing to pleural adhesions, might have kinked some one of the great abdominal veins so as to produce stasis and ascites.

Against cirrhosis was the early appearance of swelling in the legs and the moderate amount of alcohol ingested. Against tuberculosis was the negative tuberculin reaction and the low gravity of the fluid obtained by tapping. On the other hand, the cell count in the fluid, the appearance of the stools, as well as the old history of pleurisy, made tuberculous peritonitis a possibility. On the whole, cirrhosis seemed the more probable, and on operation, September 18, this was found.

The patient died September 29, and autospy showed the ordinary lesions of cirrhosis of the liver, and in addition a thrombosis of the portal vein and a chronic peritonitis. There was also slight fibrous endocarditis of the aortic and mitral valves and slight hypertrophy and dilatation of the heart. There was obsolete tuberculosis of a tracheal lymph gland, which is interesting in view of the negative tuberculin reaction.

CASE II.—*Effusion in the left chest and in the abdomen, with chronic cough, in a woman, aged thirty-eight years; loss of 20 pounds in weight; hypogastric tumor, believed to be uterine fibroid; operation showed fibroid of the ovary, no peritonitis; complete and lasting recovery.*

A married woman, aged thirty-eight years, entered the hospital October 9, 1908. She has previously been well except that she has had a cough since she was a girl, and had typhoid fever ten years ago. For two or three years she has felt something wrong in the pelvis, and a year ago her doctor found a uterine fibroid there. The patient thinks this tumor has been present for four years.

Seven months ago she consulted a physician for pain in her left chest. He found pleural effusion, and withdrew 2 quarts of fluid by tapping. The same amount was withdrawn four weeks later, but the fluid again recurred.

A month ago the abdomen was noticed to be swelling, and this has increased up to the present time. She has had dyspnea on exertion for many years, but this has been worse within the last seven months, and now she cannot lie down flat. For the last two days the feet and legs have been swelling. The bowels move five to eight times a day during the last few weeks. Several examinations of the urine and several of the sputa have been negative.

Physical examination verified the findings of fluid in the left chest and in the abdomen. October 10 the abdomen was tapped and 18 pints of serum withdrawn. The specific gravity was 1018, and the cell count showed 63 per cent. of lymphocytes.

After tapping, a rounded solid tumor could be felt in the median line, apparently connected with the uterus, hard and painless. The diagnosis was believed to be tuberculous peritonitis, and the experiment was tried of withdrawing 8 ounces of fluid from the chest every two or three days, in order to prevent recurrence such as was

thought likely to follow if the whole amount was removed at once.

On November 21 the abdomen was again tapped and 18 pints again removed. This amount had accumulated in forty-two days, being at the rate of 7 ounces a day. After this tapping, pelvic examination showed a mass filling the pelvis, pushing the cervix up behind the pubes, very hard, irregular, non-elastic, and continuous with the suprapubic tumor. Dr. M. H. Richardson believed the condition to be one of tuberculous peritonitis with a concomitant uterine tumor, benign or malignant.

The association of fluid in the abdomen with fluid in the chest, and the history of a chronic cough, together with the high gravity of the fluid, made us confident of the diagnosis of tuberculous peritonitis, although in the two and one-half months of her stay in the medical wards there was never any fever. The blood and urine were throughout negative, as was the rest of the visceral examination.

Operation, December 12, showed no peritonitis, but a fibroma of the ovary; after the removal of this the patient convalesced rapidly, and when I saw her a year later she was in perfect health, as she had been for the last eleven months since leaving the hospital.

CASE III.—*Fluid in the abdomen and in one chest; general abdominal tenderness, soon passing off; positive reaction to tuberculin; no fever at other times; operation shows tuberculous peritonitis; presumable involvement of the pleura and of the left lung.*

An unmarried Italian girl, aged seventeen years, entered the hospital October 17, 1908, for enlargement of the abdomen, with fever and general abdominal pain. These symptoms had been present for the last two weeks, and had been accompanied by a dry cough.

On examination there was dulness and harsh breathing throughout the left lung except at the bottom of the axilla and the base posteriorly, where breathing was much diminished and resonance almost absent. Below the second left interspace were fine and medium crackling rales in front, and the same rales were heard below the angle of the scapula behind. The abdomen showed all the evidences of free fluid. Otherwise, physical examination was negative, and the blood and urine showed nothing abnormal.

After the first five days the patient had practically no fever throughout her two months' stay in the hospital. The abdomen showed general tenderness, but was otherwise negative, save for the evidences of free fluid above referred to. The abdomen was tapped on the 21st, and only a few ounces of clear serous fluid obtained. Five mg. tuberculin were injected subcutaneously on the 30th, after which the temperature rose from normal to 103.2° within six hours, returning to normal within twelve hours more. The cutaneous reaction for tuberculosis was also positive.

She gained weight, although there was no increase in the amount of fluid, and on November 12 was allowed to go home. After this she slept out of doors and lived out of doors continuously, but by January the abdomen began to enlarge again, and January 16 she was operated on and diffuse tuberculosis of the peritoneum found. Diagnosis was verified by microscopic examination of an excised piece. The Fallopian tubes were also tuberculous, and were removed. Convalescence was uneventful.

The resemblance between this case and that last described is striking. Indeed, but for the presence of the tumor in the first case, the abdominal tenderness and the scantiness of the ascites in the second, they are almost identical from a clinical standpoint, despite the entire difference of the acutal pathological condition present.

A relatively slow accumulation of fluid and a slight general rigidity and tenderness of the belly help to distinguish the ascites of tuberculous peritonitis from that produced by other diseases.

CASE IV.—*Ascites and edema of the legs appearing as the only symptom in a boy, aged six years; urinary findings as of chronic glomerulonephritis; rapid reaccumulation of the fluid, necessitating tapping every two weeks; no other symptoms of importance.*

A boy, aged six years, entered the hospital October 19, 1908. His history was not of significance up to five months previously, when his abdomen began to swell; there was also some puffiness of the face, but no other symptoms, and within a few weeks he was able to be up and about. Later, he relapsed, and two months ago the abdomen was tapped, 4 quarts of dark yellow, turbid fluid being withdrawn.

Since this there has been considerable vomiting, and at one time he had convulsions and was considered moribund. He was tapped again three weeks ago and 3 quarts of fluid withdrawn. Since then the abdomen has rapidly refilled.

On examination the heart impulse was in the nipple line, fourth space. The cardiac examination was otherwise not remarkable. Blood pressure not measured. The lungs were negative, the abdomen very prominent, showing all the evidences of free fluid. Considerable soft edema of the legs and feet.

The urine averaged between 5 and 10 ounces in twenty-four hours, during his stay in the hospital. The specific gravity was between 1020 and 1022; the amount of albumin from 0.5 per cent. to 0.9 per cent. In the sediment were many hyaline, granular, and fatty casts.

The abdomen was tapped on October 21, and 5 quarts 6 ounces of chylous fluid withdrawn; specific gravity, 1009. In the sediment, lymphocytes, 37 per cent.; epithelial cells, 63 per cent.

The boy left the hospital on November 2, 1908, in very poor condition, and remained so until February, 1909, when, after

tapping, his abdomen did not refill, and this improved condition persisted for three months. Since then he has had to be tapped every two weeks, fifteen times in all, up to September 27. (An average accumulation of about 12 ounces a day.)

His condition in September, 1909, was in all respects essentially the same as it had been a year before, except that the heart was 1.5 cm. farther to the left. He was tapped on the 28th and 5 quarts (5800 c.c) of opalescent fluid removed; specific gravity, 1006. After this the fluid reaccumulated very slowly, and he was allowed to go home on October 9.

CASE V.—*Alcoholic cirrhosis of the liver in a man, aged thirty-nine years; two and one-half months duration; omentopexy; no recurrence of ascites during the period of one year thereafter.*

A dentist, aged thirty-nine years, entered the hospital October 20, 1908. He had been in the habit of taking a pint and a half of whisky a day for the last two years, and an unknown amount for eight years previously. Two and one-half months ago he noticed that his trousers were tight around the waist. This increased so rapidly that four weeks later the abdomen had to be tapped, and 5 quarts of serous fluid were withdrawn. Since then he has been tapped four times, the amount being about the same each time. This means an accumulation of about 16 ounces a day. His feet have never been swollen, his appetite has been good, there has been no pain or other symptoms of any kind. The last tapping was a week ago.

Physical examination was essentially negative except for the evidences of ascites. The blood and urine showed nothing abnormal. Temperature, pulse, and respiration were normal. October 27, 14 pints 7 ounces of turbid yellow fluid were withdrawn. After tapping, the edge of the liver could not be felt below the ribs, but could be touched by reaching up behind the costal margin. The specific gravity of the fluid was 1008.

On October 28 the abdomen was opened, the liver found to be shrunken and irregularly nodular. Omentopexy was done, but by November 9 the patient had to be tapped again, and 9 pints of fluid were removed. (Rate of accumulation, 12 ounces a day.)

He left the hospital on November 22, 1908. November 29, 1909, the patient was seen and seemed to be in excellent condition. There was no return of fluid in the abdomen. The abdomen was tapped within a few days after his leaving the hospital in November, 1908, but tapping has not been required since. He now eats well, sleeps well, and looks well.

CASE VI.—*Ascites of very gradual onset, probably two years or more, in a non-alcoholic subject; no fever, no abdominal tenderness; positive tuberculin reaction; laparotomy shows no tuberculosis or cirrhosis; second operation done for cardiolysis; slight improvement thereafter; the ascites fairly controlled by energetic administration of cathartics and diuretics.*

A salesman, aged thirty-four years, entered the hospital November 13, 1908. His family history and past history not remarkable, habits good. For four or five years he has been gaining weight and has noticed that his trousers were tight about the waist. His usual weight is 150 pounds, now 158. The increase of his girth has been especially marked in the last year, and has been accompanied by dyspnea on exertion. During the last ten months his appetite has also failed; he has had a good deal of vomiting soon after meals, also troublesome constipation. He worked until nine months ago. Eight months ago he was tapped, and 6½ quarts of clear fluid removed. After a month he began to refill. He has been treated during the last four months in the Out-patient Department.

Physical Examination. The heart's impulse extended 2 cm. outside the nipple line in the fifth space. The heart sounds were clear and there was nothing else of interest in the cardiac condition. The position of the apex shifted outward 2.5 cm. when he lay on the left side. The peripheral arteries were normal, and the lungs negative. The abdomen showed all the evidences of free fluid, and the edge of the liver could be felt 7 cm. below the costal margin in the mammary line.

He was tapped November 20; 202 ounces of yellow turbid fluid removed; specific gravity, 1020. In the sediment 85 per cent. of small lymphocytes, 15 per cent. of large lymphocytes. Nothing more felt after tapping. After an injection of 0.005 tuberculin subcutaneously there was a positive temperature reaction. The *x*-rays showed no evidences of tuberculosis in the lungs. At this time the spleen was easily palpable when the patient lay upon his right side, and it was noticed that there was a systolic retraction of the apical and precordial region. Adherent pericardium, tuberculous peritonitis, and cirrhosis were considered, but laparotomy December 5 showed no tuberculosis, and no evidence of disease in the liver so far as the surgeon's hand could discover. Dr. M. H. Richardson and Dr. Hugh Cabot considered the case to be probably one of pericarditis with adhesions and secondary ascites.

After that he got along until January 9, 1909, with two tappings, but was then operated on again, January 10, for the relief of adherent pericardium. Parts of the third, fourth, and fifth ribs were resected from their sternal attachments to a point 4 inches to the left. This seemed to allow the free retraction of the heart, and was deemed sufficient.

He returned to the medical wards on January 26, 1909, and under calomel diuresis the urine rose to 68 ounces and the amount of ascites was considerably decreased. This calomel diuresis was repeated ten days later, with success as before. On March 4 he was tapped, but only 4 quarts removed. The liver edge was then felt 5 cm. below the ribs. The specific gravity of the ascitic fluid was 1017. March 10 he was tapped again, but only 6 pints found.

A calomel diuresis was attempted on March 15, but was unsuccessful. It was evident that after the operation for cardiolysis the accumulation of ascites was slower, though this may have been due to the persistent administration of diuretics and cathartics. He was last seen March 27, 1909.

CASE VII.—A Russian Jewish millgirl, aged eighteen years, entered the hospital December 2, 1908, with a diagnosis of tuberculous peritonitis made in the Out-patient Department by Dr. W. H. Smith (O. P. D., No. 118,422). Her family history and past history were uneventful. Menstruation began at twelve and has been regular until within the last year, when it has become more frequent, and lately has come every two weeks and lasted four days each time. For three months she has noticed enlargement of the abdomen, and thinks she has been losing weight. Within the last month she has had some abdominal pain, paroxysmal and griping. Her appetite has been good and there has been no cough or other symptoms. Pulse, temperature, and respiration were moderately and irregularly elevated. The urine showed nothing abnormal. In the blood were 17,900 leukocytes per cubic millimeter December 3; 16,800 leukocytes December 7.

Physical examination was negative except as relates to the abdomen, which was prominent, tense, flat on percussion throughout, symmetrical, and gave a fluid wave. Girth at the umbilicus, 86.5 cm. The edge of the liver was not felt. No edema.

Tuberculous peritonitis was considered, but the leukocytosis and the extreme tightness of the belly made the diagnosis doubtful.

December 4 the abdomen was tapped above the pubes and 96 ounces of muddy, thick, viscid, ropy, alkaline fluid obtained; gravity, 1025. The fluid resembled very thick maple syrup and formed a jelly-like mass after heating. When diluted there was no precipitate or clot obtained by heat or by the addition of acetic acid. Biuret reaction negative. The addition of alcohol produced a heavy, ropy, tenacious precipitate (psuedomucine and paramucine). This precipitate, when boiled with acid, broke up into two bodies, one of which reduced Fehling's while the the other gave the Biuret reaction. In the sediment there was nothing distinctive. The fluid was obviously characteristic of the contents of an ovarian cyst. By laparotomy a large multilocular cyst of the right ovary was removed without incident.

CASE VIII.—A housewife, aged thirty-seven years, entered the hospital February 15, 1909. She had had a miscarriage seven and one-half years ago, purposely induced; one living child five years old. Two threatened miscarriages in the course of this pregnancy. The baby was anemic for the first three weeks, but otherwise has been well. The patient had diphtheria twelve years ago, and the throat was sore for six weeks at that time. Three years ago began to have pains in her lower legs, especially along the

shins. The pains came at night, were very severe, and prevented sleep. There were no enlarged veins or other noticeable changes, but the bones were sore to the touch. A year later some ulcers appeared; the last one healed three months ago. Four months ago she had severe pain in the occiput, worse at night, and at this time three lumps appeared on her head about one inch in diameter, sore to the touch. One of them still remains.

Since her last pregnancy has had trouble with her nose, causing difficulty with breathing. At this time also, about five years ago, her hair came out profusely for a time. Two or three years ago she noticed a tumor in her left hypochondrium, which caused no symptoms, but bothered her in putting on her corsets. Last October she was operated on for hemorrhoids, and at that time the doctor said that her spleen was enlarged.

Two and one-half months ago the belly began to enlarge, and she has been tapped twice, six weeks ago and three weeks ago. On examination there were many pea-sized bilateral cervical glands. Chest was negative; blood pressure, 135 mm. The upper border of the liver showed on percussion a median elevation just above the nipple line. The edge of the spleen was felt 12 cm. below the ribs. There was evidence of free fluid in the abdomen, and the girth at the umbilicus was 109 cm. Considerable soft edema of the ankles, and dark brown scars over the ankles and shins. On the forehead near the hair line a slight periosteal thickening, and another higher up in the hair on the frontal bone. *X*-ray plates show specific changes in the tibiæ. Under antisyphilitic treatment and diuretin the patient improved rapidly. The fluid diminished in amount, but on March 2, 6 quarts were withdrawn, after which the edge of the liver could be easily felt 2 cm. below the ribs in the nipple line. The ascitic fluid was 1009 in specific gravity and showed 90 per cent. of mononuclear cells, about one-half of them large and one-half small. She left the hospital March 6, 1909, and up to date, May 1, 1911, has remained well.

Case IX.—A shoemaker, aged fifty-three years, entered the hospital November 12, 1908. Family history and past history not remarkable. Eight years ago lumps appeared in the left side of his neck, and have not changed since then until a year ago, when additional and larger lumps made their appearance near those previously felt. Also similar lumps in the axillæ and groins. Nine months ago lumps were noticed in the abdomen. Three weeks ago the belly and legs began to swell, and a week ago he was tapped in the Out-patient Department and 2200 c.c. removed; specific gravity, 1011; sediment lymphocytic. Eighteen months ago he weighed 180 pounds, a month ago 160 pounds. A gland was removed in the Out-patient Department, and a diagnosis of lymphosarcoma made.

On physical examination there was a mass of glands, roughly 10 by 8 cm., in the left side of the neck, not adherent to the skin,

and fairly movable. Elsewhere in the neck, axillæ and groins there were glands from the size of a bean to that of a hickory nut. The right pupil slightly larger than the left. Heart's apex, 1.5 cm. outside the nipple line. Cardiac examination otherwise not significant; lungs negative. The abdomen showed evidences of free fluid and large irregular tumors. The spleen and liver not made out. On the posterior rectal wall a mass half the size of the fist, hard and nodular, was palpable.

He was tapped on November 25 and 82 ounces of brownish-red fluid obtained. On December 4, 86 ounces more were removed. Specific gravity, 1015; sediment mostly epithelial cells. December 8, 115 ounces more were withdrawn. December 20, only 12 ounces. December 24, 17 ounces more. December 28, *x*-rays showed shadow over the whole left side of the chest.

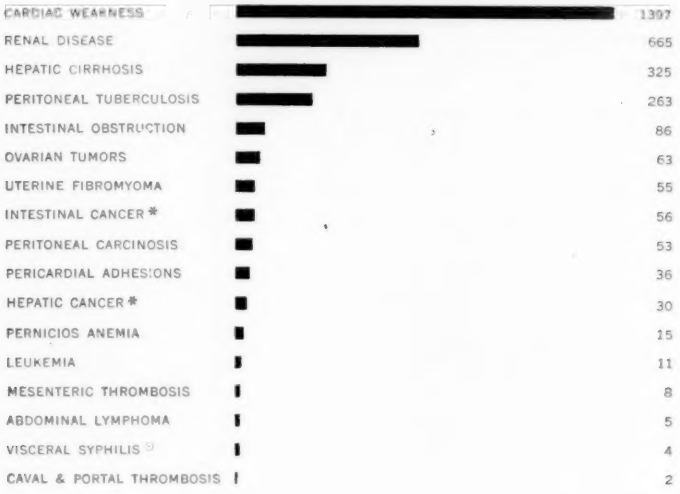

CHART I.—Relative frequency of the common causes of ascites as observed at the Massachusetts General Hospital (1870 to 1910).

Under diuretin, started December 26, urine rose on the 30th to 62 ounces, and several times subsequently 60 to 80 ounces were obtained as the result of diuretin. He was tapped December 28, and 7 pints obtained. On January 3, 50 ounces; January 9, 6 pints; January 15, 106 ounces; January 19, 96 ounces. He left the hospital January 21, and died soon after at home.

SOLID TUMORS OF THE OVARY.

1. *Cancer of the Ovary.* Fifty-four cases are on record at the Massachusetts General Hospital between 1870 and 1910. In 6 of these there was no operation or autopsy. Of the remaining 48, there were 19 cases (40 per cent.) in which a considerable amount of ascites was found.

2. *Fibroma of the Ovary.* Twenty well-recorded cases are to be found in our records. In 10 of these (50 per cent.) ascites was well marked at the time of operation.

3. *Sarcoma of the Ovary.* Five cases, one with ascites.

CYSTIC TUMORS OF THE OVARY.

There were 391 cases operated upon at the Massachusetts General Hospital (1870 to 1910) for multilocular ovarian cyst. In 31 of these, or 7.9 per cent., ascites was well marked at the time of operation. In 8 of these 31 the fluid was bloody or chocolate colored. In 1 the amount of serum was measured at 17 quarts.

TABLE III.

Disease.	No. of cases.	Rate of ascitic accumulation. Ounces per day.
1. Cardiac weakness	2	36–54
2. Cirrhosis of the liver	16	20
3. Chronic nephritis	5	13
4. Solid tumors of ovary	2	12
5. Neoplasms of the abdominal organs and glands	4	11
6. Adherent pericardium (before cardiolysis)	2	11
Adherent pericardium (after cardiolysis)	1	2
7. Uterine fibroid	2	8–11
8. Tuberculous peritonitis	15	5– 6

TABLE IV.—Percentage of Ascites Occurring in the Different Varieties of Ovarian Tumor.

Diagnosis.	No. of cases.	Ascites found at operation in
Ovarian fibroma	20	50 per cent.
Ovarian cancer	54	40 per cent.
Ovarian sarcoma	5	20 per cent.
Ovarian cystoma	391	7.9 per cent.

Among 14 cases operated upon for *parovarian cyst* no ascites was found in any.

UTERINE FIBROMYOMA.

Among 723 cases operated upon for fibriod of the uterus, 55 cases, or 7 per cent., showed ascites. This was of small amount in 18 cases (2.4 per cent.); of large amount in the remaining 37 (4.6 per cent.).

In 10 of the 55 cases the fluid was bloody; in 2 others it was purulent.

In Table IV the relation of ascites to the different varieties of ovarian tumor is demonstrated. All these cases were operated on. I think many persons will be surprised, as I was, to learn how frequent is the association of ascites with benign ovarian growths such as fibroma and multilocular cyst. I have no idea why a small ovarian fibroma without metastases should produce extensive ascites so frequently.

Why should a small percentage (7.9 per cent.) of cystic tumors produce ascites? One would expect to find it in all cases or in none.

SUMMARY AND CONCLUSIONS.

1. Among the possible causes of extensive ascites we must not lose sight of the small solid tumors of the ovary.
2. Pleural effusion may be produced by an extensive ascitic accumulation. This association may lead to a false diagnosis of pleural and peritoneal tuberculosis.
3. The cure of both pleural and peritoneal effusions may result from excising a benign ovarian tumor.
4. Among all causes of ascites, tuberculous peritonitis may sometimes be recognized by the greater slowness of its accumulation of fluid.
5. Intestinal obstruction ranks fifth and disease of the female genitals sixth among the causes of ascites, being surpassed only by cardiac disease, nephritis, cirrhosis, and tuberculous peritonitis.
6. Besides the causes just mentioned, abdominal neoplasms and adherent pericardium are the only factors of importance in the production of ascites.

INFANTILE HYPERTROPHIC STENOSIS OF THE PYLORUS, BASED UPON A PERSONAL EXPERIENCE OF SEVEN OPERATED CASES.

By Frank E. Bunts, M.D.,

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From the first publication of a case of infantile pyloric stenosis by an American physician, Hezekiah Beardsley, in 1778, to the time of the publication of the Danish physician Hirschsprung's 2 cases, in 1887, little or no attention had been given to this important

and somewhat frequent malady of infancy, but with each succeeding year reports of cases are now multiplying, till what was once considered a rare disease is now coming to be recognized as of frequent occurrence, and our profession generally is growing fairly well acquainted with the clinical phenomena connected with it.

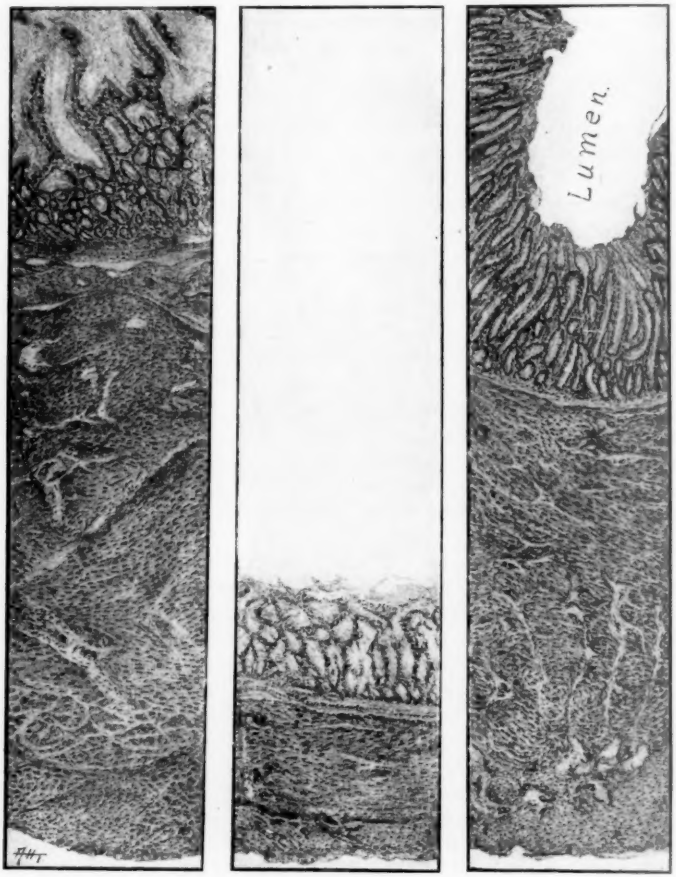
Evidently, however, it is either not recognized as frequently as it should be, or a decided feeling against operation must exist, since in a city the size of Cleveland but 9 cases, so far as I am aware, have been operated upon during the last five years. It is almost useless to go into the statistical results of operations for infantile stenosis of the pylorus, since, notwithstanding the increasing number of operated cases, the average mortality remains in the neighborhood of 50 per cent. It is to be noted, however, that in the hands of those whose number of cases is large, the mortality is decreasing slightly, and this may be ascribed to two causes—first, though not in my estimation the more important, because of increasing familiarity with the details of the operation and improved technique; and second, and of great importance if true, because physicians have had their attention called to the matter until they are quicker to recognize the symptoms and to urge operation, so that occasionally an infant is brought for operation that is not nearly moribund at the time. The laity must always be an obstacle to early operation, for marasmus is a well-known condition, and the feeling that a proper diet will correct the trouble will often prevent their consenting to an interference early enough to be of any avail.

Because of these considerations, it seems to me that it is proper to present some of the facts pertaining to this interesting and important infantile anomaly. My observations rest upon a study of 7 cases operated upon by myself, of which 4 lived and 3 died.

First, as to the pathological anatomy. It might seem that the stomach would be greatly dilated as a result of the pyloric obstruction, and while such cases have been reported, it is not uniformly so. In none of my 7 cases was there extreme dilatation. Some cases have, on the other hand, been reported in which the stomach was contracted to approximately one-half of the normal size. It is conceivable that this is due to the persistent and easy vomiting which does not permit of the stomach becoming habitually overdistended, and it may be that the greatly exaggerated musculature of the pylorus, by its almost complete obstruction, causes the much weaker cardia to give way and allow of easy regurgitant vomiting.

The pylorus itself is enlarged for a distance of nearly an inch, is pale and glistening in appearance, and has the consistency and feels on palpation much like the cervix uteri; so hard, indeed, that it is often compared to a piece of cartilage. Macroscopically, on cross-section, there is an exaggerated muscularis with a mucosa thrown into folds which in some cases completely block egress

from the stomach into the duodenum. Microscopically, as shown in the accompanying drawings (Figs. 1 and 2), a cross-section of the pylorus shows the following changes: (1) Almost complete



1 2 3

FIG. 1.—Microscopic sections of pylorus: 1, pyloric stenosis with no lumen; 2, normal pylorus; 3, pyloric stenosis in infancy with a lumen.

obliteration of the lumen, so that only a pin-point aperture exists. (2) The mucosa and submucosa are thrown into four folds by the contraction of the underlying muscle, and this seems to be the cause of the obliteration of the lumen. (3) There is a great thickening of

the circular muscle layer, and some fibrosis. (4) The other layers do not seem to be greatly changed, although some slight increase in the size of the longitudinal band of muscle is also to be noted, and a slight catarrhal inflammation of the mucosa. The muscular bundles in the submucosa do not appear to be increased.

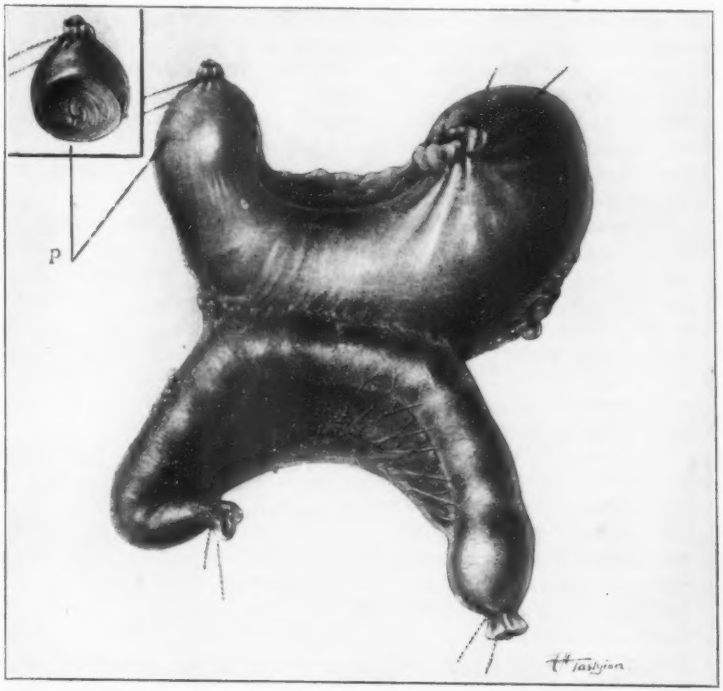


FIG. 2.—Pyloric stenosis in infancy with complete occlusion (*p*). This specimen was obtained from a patient on whom a gastro-enterostomy had been performed.

While the enlargement of the pylorus may, in its appearance and consistency, resemble a tumor, it is, as has been conclusively shown in numerous specimens, purely an hypertrophy, though in a rare case reported by Dent an aberrant portion of pancreas was found situated beneath the pyloric mucosa, and Torkel found situated beneath the submucosa an abnormal glandular structure which he considered to belong to a wandering Brunner's gland. Important contribution to our knowledge of the pathology of this condition has been made by Ibrahim and others by the examination of the stomachs of infants who had recovered under medical treatment from what had been clinically diagnosticated as pyloric stenosis,

and died from other accidental causes. In these it was shown that the pyloric hypertrophy still remained, but that there had been developed a compensating hypertrophy of the stomach walls.

This observation has led Fredet and Guillemot to believe that in hypertrophic stenosis the organic lesion is not all, and that we must give a large place to secondary factors such as spasm, and to tumefaction of the mucous folds. On this basis it is easy to comprehend why and how the hypertrophic stenosis might not manifest itself until long after birth, and to answer the most serious objections to the theory of the malformation being of congenital origin. They also think that this explanation does away with the claim that hypertrophic stenosis cannot be cured by purely medical treatment, and that such reported cases of cure do not belong to the class of cases described by Hirschsprung.

While the evidence at hand at present is not sufficient to prove definitely that a true infantile as distinguished from a congenital hypertrophy of the pylorus does not exist, yet it seems probable that the latter hypothesis may well explain all the phenomena present.

The symptoms are of the greatest importance, for it is only by their early recognition and interpretation that we may expect to secure operative interference at a time when we may expect to lower materially the percentage of mortality. I believe that operative procedures have established their value as a life-saving measure. It remains now to secure the coöperation of the physicians and the laity in securing the operation at an early and favorable time. Naturally, the first symptom to attract attention is vomiting. This may not make its appearance for several weeks after birth or may begin with the first nursing. It seems to matter but little whether the child is breast fed or bottle fed, the cause is equally operative. At first the vomited matter represents but part of the ingested material, but eventually, notwithstanding every art of infant feeding, every mouthful of food is apparently ejected. Sometimes there will be a few hours or a day when the retention of a portion of the feeding will bring false hopes of recovery, to be followed, however, by the same distressing symptoms. In such cases we may imagine that the mucous folds of the pyloric outlet have become a little less congested, the opening a little less constricted, thus allowing a temporary escape of fluids. With the persistent vomiting we have a progressive emaciation of the infant, so that a child weighing eight or ten pounds at birth may weigh not over five or six pounds when it comes to operation some six weeks later.

If we can rule out the possibility of the vomiting being purely reflex from some other disease, it becomes of very great diagnostic importance. The absence or a small number of bowel movements soon becomes a marked symptom, and gradually the development of anuria is noted.

A symptom of the greatest importance, but one likely to be overlooked while the baby is fat and plump, is the dilatation of the stomach followed by a marked wave of contraction plainly visible as it travels toward the pylorus. In the greatly emaciated and delayed cases this phenomenon is peculiarly well marked, and may be watched as it arises spontaneously or may be brought into action by sharp palpation over the stomach. This ball-like tumor, with its peristalic wave is so marked as to be readily made out by the nurse or mother.

It might be thought that the pyloric tumor would be readily palpable, but from my own experience such was not the case, for in only 2 out of 7 was I able positively to identify it. So that while its presence must be considered of the greatest significance, its absence in the presence of other confirmatory symptoms, is not to be seriously considered as evidence against the stenosis being present.

In their order, then, of importance, ruling out reflex disturbances, I would place the symptoms as: (1) Persistent vomiting, (2) emaciation, (3) visible dilatation of stomach, (4) visible peristalsis of stomach, (5) diminution and absence of stools, (6) anuria, (7) presence of palpable tumor of pylorus.

Colored powders incorporated in the food and absent from the stools might help in the diagnosis of pyloric obstruction, but I have not had an opportunity to make use of this method. In deciding for an operation one must take into consideration that the relatively early appearance of the symptoms mentioned speaks for organic rather than spasmodic stricture, and also that the latter condition should speedily respond to proper medical treatment.

The percentage of recoveries after operation has not been particularly gratifying (from 50 to 60 per cent.), if we consider it from the standpoint of percentage alone, but if we consider that these cases when they come to the surgeon have almost uniformly received long continued and varied medical care, and have reached the stage where it seems almost incredible that any of them should recover from gastro-enterostomy, then the percentage of recoveries does not seem unfavorable. They are emaciated, starving, and dying of thirst, and yet not only a severe operation must be gone through, but the extremely difficult problem of nourishment in the face of all these obstacles must be solved and solved quickly to save the infant.

The prognosis will improve as earlier diagnosis is made and earlier consent of parents to operation obtained. It would, I believe, be highly desirable to have a surgeon see suspected cases in consultation with the physician, not with a view to immediate operation, but in order better to arrive at an harmonious conclusion as to the safe and imperative time for surgical intervention. That even under the unfavorable existing obstacles to early operation improvement in the last three years has taken place, is shown by the results

in 38 such cases collected by Fredet and Guillemot, in which the mortality was but 26.31 per cent.

In my own series of 7 cases, 4 have recovered and are still living. In only 1 of these was the patient what might have been termed a fair operative risk. In only 1 of the 3 cases that died did I succeed in getting an autopsy. This was in an extremely feeble and emaciated child in which we had detected mesenteric tubercles at the time of operation. The child lived forty-eight hours, and died without any rise in temperature or other disturbances, probably from sheer exhaustion.

The drawings herewith presented are taken from this case and also from an apparently normal pylorus in a child ten days old dying from esophageal obstruction. One of the other deaths might possibly have been due to too severe crushing of the stomach or intestine with clamps (used in the first 2 operations) though of this I cannot, of course, be perfectly certain. The other lived eighteen hours, and died very suddenly after a convulsion and sharp rise in temperature.

My own conviction is that with even reasonably promising cases the mortality should be in the neighborhood of 25 per cent. but I do not believe that this reduction in mortality will be due very largely to an improved technique, but rather to securing patients at an earlier and more favorable time.

Regarding the technique, ether has been used in each case. It has been sought to retain the body heat by cotton wadding bandaged about the limbs and by warm water bags under the operating table pads. The incision has been slightly to the left of the median line, and has extended down to or below the navel, in one case enabling me to relieve an epigastric hernia at the same time. In some of the cases the stomach was previously washed out, but even then I found the stomach tensely distended with gas and a considerable amount of curds poured out when the stomach was opened. This distention of the stomach is quite annoying until the stomach has been opened.

Notwithstanding certain theoretical advantages in the posterior anastomosis, I have done the anterior operation in all the cases, making a long loop, but not doing an additional anastomosis between the two limbs of the jejunum. My reason for adhering to the anterior operation in these cases has been a fancied lessening of the shock due to the lessened exposure of the abdominal viscera, and to the somewhat increased ease of operation when the stomach is dilated and tense. Personally, while I now habitually perform the posterior no-loop gastro-enterostomy in adult patients, I have never been convinced that the results were in any way superior to those obtained by the anterior method, so that if the anterior operation offers any advantage either in facility or safety, it seems to me proper to make use of it.

The closure of the abdominal wound is of considerable importance, for in a number of reported cases the line of incision has given way under the severe and uncontrollable straining of a crying infant, and the intestines protruded through the opening. In hope of preventing this I have used the chromic catgut sutures for both muscles and peritoneum, and reënforced these by silkworm-gut sutures through the entire thickness of the abdominal wall, removing part of them at the end of eight days and the remainder in ten to twelve days.

Feeding the child is of the very greatest importance, and I am much indebted to the physicians who have been associated with me in these cases for the valuable suggestions which have enabled me to formulate a general plan of attempt at nourishment that has proved fairly satisfactory. Sterilized water may be given, a teaspoonful at a time, as soon as the effects of the ether have passed off, and on the following day albumin water may be given in small amounts frequently repeated. For the first three days, however, most reliance must be placed upon rectal feeding, peptonized milk being used for this purpose at four-hour intervals. Whenever the mother's milk can be obtained, it should be used for this purpose. At the end of two to three days the stomach will be sufficiently quieted to permit of the addition of whey, and then mother's milk or modified milk in small quantities to the albumin water; and in exceptionally favorable cases the babe can be put to the breast to nurse for short periods.

No fear of leakage along the line of sutures need be felt if the operation has been thoroughly performed and the amount of nourishment given at any one time is small in quantity. The food is gradually increased as the condition of the child demands it, and the whole body rubbed with sweet oil from time to time to aid, however slightly, in the nourishment of the infant.

Dr. Scudder has made an elaborate and valuable study of the conditions following recovery, especially as to the metabolic changes, and, in a general way, these infants seem to do as well as others of the same age. The earliest of my own cases is now over four years old, and is as strong and hearty as any child could be expected to be. My third case is nearly three years old, and in perfect health. The fifth is one year old, and in excellent health. While the seventh and last is but seven weeks old, it has passed through the crisis of operation and feeding, and is gaining at the rate of about two ounces per day.

In concluding these fragmentary observations I beg again to call attention to the symptoms of the pyloric obstruction, and to the great importance of its early recognition, and appreciation that surgery offers a really brilliant prospect for its relief in properly selected cases.

LEUKEMIA IN CHILDHOOD.

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Three cases of leukemia in young children have been observed by the writer within the space of two years. Their histories were as follows:

Case I.—A girl, aged five years, living in Fresno, California, was brought to me in January 1909, referred by Dr. J. L. Maupin. Her past history was as follows: She had no illness of any kind until three years of age, when she passed through a protracted fever, six weeks in duration, diagnosed as malaria. In May, 1908, she was taken on a visit to Georgia, and there had mumps and chickenpox in light form; she recovered from these and returned to Fresno in June, but since that time she never seemed quite well.

Her present illness dated back to the Georgia trip, ever since which she had gradually grown paler, tired easily, and seemed breathless on exertion. But she never appeared seriously ill until an attack of tonsillitis two weeks previous to my seeing her, in which there was high fever and much swelling of the tonsils. From that time on she remained very weak and exhausted.

Physical examination showed the child to be very white, but well nourished. The lymphatic glands were moderately enlarged in both sides of the neck, both axillæ, and both groins. The spleen measured 10 cm. in area in the anterior axillary line, and the lower edge was distinctly palpable. The liver measured 12 cm. in the nipple line and its lower border was palpable half-way to the navel. The lungs were apparently normal. The heart showed a loud systolic murmur at all orifices, but the second sound was clear. The pulse rate was 140. A number of black and blue marks, the size of a bean, were visible over both shins and calves; and numerous smaller purpuric spots, petechial in character.

The urine was clear and showed no albumin or sugar. Blood examination, made on January 6, showed as follows: Hemoglobin, 21 per cent.; red corpuscles, 1,500,000, irregular in shape and size, poor in coloring, none nucleated, no malarial parasites; white corpuscles, 19,000; no polymorphonuclears; small lymphocytes, 96 per cent.; large lymphocytes, 4 per cent. On January 11 a second examination showed: Hemoglobin, 20 per cent.; red corpuscles, 1,150,000; white corpuscles, 14,000; small lymphocytes, 97 per cent.; large lymphocytes, 2 per cent.; polymorphonuclears, 1 per cent.; moderate poikilocytosis, polychromatophilia, numerous megalocytes.

Outcome. The child rapidly grew worse, with restlessness, drowsiness, delirium, refusal to eat; temperature, 101° to 103° by

rectum; pulse, 130 to 140; and died on the evening of January 11. The whole illness was apparently only six months at most in duration.

CASE II.—A boy, aged four years and five months, living at Santa Maria, Cal., was referred to me in June, 1909, by Dr. L. Bert Coblentz. The child had always been perfectly healthy before, never had had any of the diseases of childhood, or an illness of any kind. He had never been noticed to ail until about two weeks before I saw him, when he began to complain of pain in his left side, under the ribs. He also said he felt tired, and was not inclined to play. The pain, lassitude, and weariness gradually increased, and the boy grew pale, sallow, and breathless, so that he panted on slight exertion. The most noticeable feature had been his indisposition to play, and his weariness and lassitude; previously active and vivacious, he now cared only to lie down and rest.

Physical examination showed a boy well nourished, apparently well, tanned by the sun, bright and happy in manner. All superficial glands were found palpably enlarged, though none larger than a cherry, and all freely movable. The spleen was enlarged downward, with the notches plainly palpable along its lower edge, the free border extended to the level of the navel, and the total area of dulness measured 14 cm. The lungs and heart showed no abnormality, and the urine was clear. Over each arm and over the abdomen there were a number of small black-and-blue marks.

The blood showed: Hemoglobin, 45 per cent.; red corpuscles, 2,500,000; white corpuscles, 304,000; polymorphonuclears, 2 per cent.; large lymphocytes, 2 per cent.; small lymphocytes, 96 per cent.

This boy died on July 19, just six weeks from the time the first sign of his trouble was observed. His last two weeks were days of great distress from the splenic enlargement and pressure, with shortness of breath, nausea, constant moaning, apparently great pain, and finally delirium and coma.

CASE III.—A boy, aged seven years, living in Colusa, California, was referred to me in June, 1910, by Dr. C. A. Poage. The child was exceptionally well until two years of age, but he then had an illness diagnosed malaria, characterized by chills and fever, treated with quinine, and apparently cured. He had never seemed well since then, but had never had any definite attack of malaria, though he frequently had spells of fever, always disappearing in response to quinine. Three weeks before he was brought to me he had another attack of fever, seemed drowsy and weak, was supposed to have malaria again, and was given quinine. But this time his fever persisted, and he did not improve. Then it was discovered that his abdomen was enlarged. He had continued to be up and about, but tired easily, and had lost his appetite.

Physical Examination. On examination the child was found to be very pale, but fairly well nourished. The abdomen was distended

and protuberant, and showed many dilated veins. The spleen was greatly enlarged, occupying the left half of the abdomen, the lower border extended 5 cm. below the level of the navel, and the notches were distinctly palpable; but the right border did not pass the median line. The liver was likewise enlarged, measuring 12 cm. in its area of dulness, and its lower border being palpable 5 cm. below the costal margin. The lungs were clear throughout. The heart showed no evidence of disease except a loud systolic murmur over the pulmonic orifice. The pulse rate was 140, the temperature 100°. There was in this case nowhere any enlargement of superficial lymphatic glands.

The blood showed a hemoglobin percentage of only 15; the red corpuscles numbered 2,000,000, varied greatly in shape and size, were very pale, and a few nucleated reds were found; the white corpuscles numbered 480,000, of which the small lymphocytes were 96 per cent.; the polymorphonuclears, 3 per cent.; the eosinophiles, 1 per cent. This boy for a time apparently improved under treatment with iron, arsenic, and *x*-ray applications over the spleen and the long bones; the spleen reducing in size, the hemoglobin and red corpuscles increasing, while the white corpuscles decreased. But after that he rapidly relapsed, and death took place on September 16, about four months from the onset of the symptoms.

These cases, when analyzed, all resemble each other closely. No one would hesitate to diagnose them as leukemia. Probably every one would agree that they belong to the lymphatic type; and from the standpoint of duration all would be classed as acute. All took the usual course, uninfluenced to any extent by treatment, toward a fatal termination. The diagnosis means death and we know no way to avoid it. To any one who cares for his profession it is heart-breaking to meet with such cases, where there is not even a chance to save life; and no doubt others like the writer have asked themselves many questions about this disease, when they had the misfortune to meet it. There are several queries particularly that crowd upon one for answer.

1. What causes it? Age does not, for leukemia occurs in every decade of life. No part of the world escapes it, and no race of people. Is it due to an infection? Or is it a form of malignant disease? Or is it of any significance or only coincidence that two of the cases herewith reported had a malarial infection preceding their leukemia, as has happened also in cases reported by other observers? Not one of these questions can be positively answered; and a perusal of the large amount of literature written on this subject during the last few years will convince any reader that there is still no adequate explanation as to what causes leukemia.

2. What is the site of the disease? Is it the lymphatic glands, or the spleen, or the bone marrow, or all three? Here again there is a vast amount of contribution and of controversy, but no certainty.

There are two main theories propounded, each of which has numerous authorities behind it. One school of Germans arrives at the conviction that every leukemia, whether clinically it be lymphatic, splenic, or mixed in type, is due to disease of all the blood-forming tissues in every part of the body; though one tissue may be more advanced in its involvement, and so determine the clinical type. A second school believes that there are two distinct leukemias, a lymphatic due to disease of lymphatic tissues all over the body, and a myeloid due to disease of the bone-marrow. Those who are interested in this discussion should read an article by Naegeli,[1] in which he reviews and dissects 156 articles on leukemia that have appeared in current literature during the past decade, mainly in German literature. After finishing Naegeli's fifty pages of text, however, one feels but little enlightened as to the truth, no matter how interested by the argument.

3. Is leukemia a common disease in children? Fortunately we can answer this question in the negative. For a long time it was believed that it never occurred except in adult life. But gradually one case after another in childhood has been reported here and there by different observers. Still the total number is small, only about 50,[2] and the disease is, therefore, an uncommon one under ten years of age. When it occurs, the great majority of cases, like those herewith reported, are of the lymphatic type and run an acute course. All observers agree that the splenomedullary type is distinctly rare in childhood.

4. What can we do in the way of treatment? Absolutely nothing that holds out any hope of cure. Arsenic, *x*-ray applications, iron, transfusion, rest, oxygen, red bone marrow, all alike have failed. There is no known remedy that seems even to stay the course of the disease. Once the diagnosis is positive, the case is hopeless. Let us be thankful that such a diagnosis does not frequently have to be made.

MANAGEMENT OF FAILURE OF THE CIRCULATORY BALANCE IN CHRONIC INTERSTITIAL NEPHRITIS.

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For the purpose of laying a foundation for an intelligent consideration of the management of failure of the circulatory balance in chronic interstitial nephritis an introductory paragraph is desirable.

[1] Ergebnisse der Inneren Medizin und Kinderheilkunde, fünfter band, 1910, p. 222
[2] Veeder, Archives of Pediatrics, January, 1911, p. 43.

The circulatory current begins with the secretion of the chyle into the intestinal lymphatics, continues through the thoracic duct, and enters the sanguineous system on the venous side near the heart, makes the lesser circuit, and is forced through the arteries and capillaries by the left ventricle. From the blood a requisite amount of nutritive material, in watery solution, is secreted through the capillary walls and enters the great extravascular circulation as tissue serum, and diffuses through the intercellular and larger serous spaces. In due course this liquid, contaminated by unused nutritive elements and waste matters, is secreted into the lymphatic radicles and conveyed through a system of ducts and purifying and filtration glands into the venous current. Portions of this liquid are also secreted into the venous ends of the capillaries and conveyed, with the surplus blood which passes the capillary barriers, through the veins to the right side of the heart. Other portions may be excreted by the kidneys, intestines, etc. The harmful materials, in aqueous solution, are directly or indirectly excreted mainly through the kidneys. The highly selective secretory and excretory functions of the specific cells of the lacteals, capillaries, lymphatics, kidneys, etc., are essentially vital, aided by the more measurable influences of composition, tension, pressure, velocity, etc., of the circulatory fluids and other physical and chemical factors. Although not demonstrable, nor indubitable, we may assume that the circulatory balance includes abundant direct and compensatory integrity and reserve capacity in circulatory fluids of adequate nutritive value, cardiac competency, vasomotor efficiency, transit-secretory activity, and other important factors.

In the cardiovascular-nephritic malady technically known as chronic interstitial nephritis there is found, in advanced cases, marked myocardial hypertrophy, arterial thickening, and renal fibrosis; the cardiac contractions are forcible, with increased resistance at the arterial terminals and great destruction of renal secretory tissue; the arterial circulation is energized, the venous flow is obstructed, and the tissue serum movement is retarded; the blood pressure is elevated, the proportion of venous blood is above the normal, and the tissue serum is largely increased in amount and altered in character. Under these circumstances the circulatory balance is deficient in reserve capacity, lacking in compensatory adaptability, delicately adjusted, and is comparatively easily broken. The loss of this balance may depend upon many factors, the majority of which are obscure or unknown. Although there may be other factors of equal or greater importance, with our present knowledge closest attention should be given to those which are obtrusively obvious, as myocardial weakness, especially that connected with insufficiency of the right auricular and ventricular aspiratory function; increased tenseness of peripheral obstruction; relative lymphatic incompetency; lessened areolar-tissue resiliency;

notable deviation from the normal composition of the tissue serum in many particulars, but especially in a diminution of the attraction, or adhesive viscosity of this liquid—in which the cells of the body may participate—by which the tissue serum is held in the intercellular spaces. It is probable that the most important of these, in the earlier stages, are venous stasis, lymphatic insufficiency, and cardiac suction failure.

Under these conditions of strain the circulatory balance is maintained partially, fitfully, and with difficulty; and often only by unconscious recourse to various devices for stimulating supplementary circulatory agencies, as, for example, a restless muscular activity, etc. In my experience manifest failure has usually followed some acute infectious malady.

Among the earliest readily recognizable signs of circulatory failure in these cases may be mentioned an increase in body weight, general plumpness, tenseness of all the tissues of the body, and an exaltation of the already high blood pressure. The face becomes fuller, and the trunk and extremities are symmetrically rounded out. Palpation reveals an increased sense of resistance, but there is no pitting upon pressure. Occult edema is present; manifest edema is imminent. The special subjective symptoms, although not robustly obtrusive, are nevertheless very significant. The physical activities of the patient are now curtailed; there is dyspnea upon unusual exertion; there is also sufficient dyspnea upon first assuming the recumbent posture to lead to the use of an additional pillow, and often this is supplemented by placing the arm under the pillows in order to further raise the head; he does not sleep as well as formerly, and occasionally he may be awakened by a severe attack of nocturnal dyspnea.

With progressive increase in the arteriocapillary obstruction and venous engorgement; with advancing myocardial weakness and dilatation; with an augmenting load of slowly moving tissue serum and lymphatic insufficiency; and after a period, which may be unexpectedly prolonged, during which there occurs a more or less urgent alignment of every primary reserve and supplementary force in an effort to sustain the toppling structure, the circulatory balance is definitely broken. The cardiac cavities are distended, probably with functional valvular insufficiency, and to the right auricular and ventricular aspiratory incompetency there is added the backward pressure of regurgitation. There is additional embarrassment in the venous circulation, especially in the liver, and dependent parts. Everywhere arteriosclerotic degenerative changes have become more marked, but especially is this true in the kidneys, where the widely spread atrophic changes in the arterioles and glomerular tufts and large increase of connective tissue produces the characteristic contracted kidney of this disease. Cellular destruction may account for the leakage of albumin into the urine.

The tenuous lymphatic radicles are compressed and, consequently and otherwise, relatively incompetent. The tissue serum is enormously increased in volume; it has become overburdened with toxic cellular wastes, and laden with an excess of salts; it is relatively, possibly absolutely, deficient in nutritive materials, and may have become notably acid in reaction; it has lost, markedly, in the quality of viscosity, and is not well held in the intercellular spaces, from whence it largely gravitates to the dependant parts, where it fills to distention the areolar tissue spaces and forms the characteristic dropsy of the "cardiac type."

The objective and subjective symptoms are prominent. There is a further increase in body weight. In the maintained upright posture the face, neck, and upper portions of the chest, parts which had been full and plump during the stage of occult edema, may be free from swelling; indeed, there may be here a noticeable deficiency of liquids. The lower limbs, genitalia, and other dependant parts are distended with dropsical fluids. In the edematous territory there is increased resistance offered to the palpating finger, and pitting follows pressure. The face and other regions from which the tissue serum has gravitated present more color than prevailed during the preceding stage, and they frequently show areas of brownish discoloration. In edema-free parts the muscles are flaccid, and there is usually absence of subcutaneous fats. As compared with earlier periods, the urine is less copious, of deeper color, of higher specific gravity, of increased acidity; it contains a larger proportion of salts, is more regularly and abundantly albuminous, and usually contains hyaline and granular casts. The blood pressure usually remains at its previous high levels. The patient is disabled. There is dyspnea upon slight exertion. He is unable to assume a horizontal position. With carefully adjusted supports he may be able to attain a more or less exaggerated semirecumbent posture; often this is impossible, and the tired sufferer obtains sleep only in various deviations from the upright position. He may be able to rest with the shoulders and head supported and inclined slightly backward. In some cases no pressure upon the back can be borne, and the patient sits erect, with or without inclination to one or the other side. In the most distressing cases he is compelled to lean forward with his head resting upon some supporting object. There may be Cheyne-Stokes respiration, frequently of slight degree; often it is typical; occasionally it is of the most distressing character. The pulse is increased in frequency and altered in character. Hemorrhages and other evidences of vascular degeneration occur. The natural course of these morbid processes is downward. Every phase of the circulatory embarrassment becomes more profound. The subjective symptoms increase in distressing features. Cerebral hemorrhage, or thrombosis, often occurs. Massive intestinal hemorrhages mark the exceptional case.

Toxemic coma or convulsions are not infrequent. Barring these and other somewhat accidental causes of death, the dropsical accumulation increases, rising higher and higher, and "when the water reaches the heart the patient dies."

Although rupture of the circulatory balance in this malady is not a common incident, nevertheless it should be considered as one of the possibilities sure to arise in a certain proportion of cases; indeed the likelihood of its appearance may be foretold with such fair assurance that the prediction may be verified by subsequent events. The recognition of the imminence, or actual presence of the lighter degrees of such failure is one of the fine arts of diagnosis; confirmed occult edema may be readily detected by any physician; the laity require no professional aid in the diagnosis of dependant dropsy.

How shall the cardiovascular-nephritic patient be protected from failure of the circulatory balance? Notwithstanding the paucity of etiological knowledge and the futility of attempts toward materially improving the pathological conditions, I am, nevertheless, of the opinion that earnest efforts along rational lines should be made toward conserving the patient's existing status, and, if possible, increasing his circulatory capacity. Not only this, but the conclusions which may be deduced from my observations are erroneous if the results of such well-directed measures are not generally beneficient.

The basic plan which I employ is, briefly, as follows: At intervals the patient is examined in such detail as to give such information as may be required concerning his environment and habits; nutritional requirements and supply; excretory capabilities and output; circulatory burden and reserve capacity. Upon the facts disclosed is based the advice given.

It is well to inform the patient that he has chronic interstitial nephritis, a malady in which the cardiac, vascular, and extravascular circulatory systems also participate fundamentally; that the disease is incurable, and the damages done are irreparable; that it is accompanied by inherent extra risks and dangers, and necessitates certain closely drawn restrictions; that, within limited bounds and probabilities, it is not incompatible with comfort, activity, usefulness, and possible long life.

The prescribed directions for diet, regimen, and medication should be based upon the requirements for the individual, as determined by the full examinations mentioned as preliminary to any advice. The diet should meet the caloric and other nutritional requirements of the patient; should consist of available foods and should be definitely formulated in terms comprehensible to the individual. The following is an example:

DIET. *Breakfast.* Take large helpings of bulky fruits, such as apples, pears, peaches, plums, prunes, cherries, strawberries, grape

fruit, bananas, melons, etc. Take an egg and two thin slices of bacon. Take an ordinary slice of bread, or an equivalent of toast, muffin, biscuit, wheat cakes, waffles, cereal, etc. Take tea, cocoa, coffee, milk, water, or carbonated water.

Luncheon. Take a very large helping of some vegetable salad, such as lettuce, tomato, asparagus, endive, etc., with a palatable dressing. There may be added pickles, olives, or other similar relish. Take a moderate amount of cheese. Take breads and liquids as at breakfast.

Dinner. Take vegetable, milk, or cream soups in variety. Take a piece of meat, fowl, fish, or game, about 2 by 2 by ½ inch in size. Take moderately of gravies. Take very freely of all kinds of succulent vegetables, as asparagus, spinach, carrots, turnips, parsnips, pease, string and Lima beans, beets, beet-tops, onions, corn, tomatoes, celery, squash, marrows, cauliflower, cabbage, Brussels sprouts, mushrooms, etc. Take moderately of potato, sweet potato, rice, and other starchy foods. Take breads and liquids as at breakfast. Take moderately or sparingly of simple desserts.

Notes. The total amount of food taken should be the smallest which will maintain nutrition at the highest level. For your purpose the best measure of this will be the maintenance of your present weight, and a sense of well being. Should there be a tendency to take on weight the quantities of bread, potato, and other starchy foods should be reduced; should the body weight decline, these foods should be taken more freely. To be sure, if, at the beginning, there should be over- or under-weight, these departures from a desirable weight should be corrected by under- or over-nutrition, continued until a satisfactory standard has been attained. As a rule, apples, peaches, pears, and similar fruits should be cooked. Succulent vegetables should be properly cooked, as should all foods requiring this process. At luncheon there may be substituted for the salad fruits, as at breakfast, or succulent vegetables, as at dinner. Under circumstances to be specifically defined from time to time, milk and cheese should be taken regularly at every meal. Upon rising, and also two and one-half or three hours after meals, take a small glass of water, or of carbonated water. There should be taken a total of from 3 to 3½ pints of liquids of all kinds during the twenty-four hours, unless specifically advised to the contrary. Avoid alcohol, foods which are notoriously difficult of digestion, and all foods which disagree.

Regimen. Take such a fair amount of active physical exercise as shall be specifically directed from time to time. Massage should replace active exercise should the latter be impracticable. Avoid as far as practicable exposure to infectious diseases; should these maladies be contracted there should be prompt and close medical supervision. Avoid tobacco. Avoid all feats of strength and

endurance; all overexertion, strain, and undue exposure. The clothing should be comfortable. Comfortable bathing with regularity, or as to be specifically directed. The body weight should be taken weekly, and recorded. Once a week all the liquids taken should be measured, as well as all the urine voided, and record made of the same. Should the bowel movements be liquid an estimate should be made of the quantity and record made of the same. Specimens of the twenty-four hours' urine, measured and labeled, should be submitted for examination once a week, fortnight, or month, as specified. Directions to be given as to the methods by which the above shall be done. Should there occur headaches, disturbances of vision, difficulties of breathing, nocturnal dyspnea, the requirement for more than one pillow in sleeping, rapid increase in weight, swelling of the feet, or any other event which is out of the ordinary, or which is not understood, consult your physician at once. Submit yourself, at the regularly appointed times, for full examination.

MEDICINAL. Once in four weeks, or as directed, take two freshly made pills of mercurial mass, of 5 grains each, every night for three days, followed the first time by half an ounce of castor oil in the morning, and the other two mornings by a saline cathartic. Other medication to be specifically directed.

Immediately upon the detection of the slightest evidences of circulatory embarrassment or occult edema, or of manifest dropsy or uremia, the patient should be given active and efficient treatment. He should be put to bed, in as nearly a horizontal position as possible, where he should remain until the circulatory balance has been restored. This I consider the most important medical measure which can be instituted, under the circumstances described, in these cases. The venous system is thus given an opportunity to drain itself easily; and the heart to regain its tone, largely because of the lessened strain upon its right-side aspiratory action, and the relief given to the ventricular contractions. In various ways probably every part of the circulatory system is offered more or less positive relief. It is usually advisable to prescribe efficient doses of an active preparation of digitalis, as, for example, the freshly prepared infusion of the best English leaves of the current year, properly gathered and preserved. At this time there should be no hesitation upon theoretical grounds pertaining to the exalted blood pressure; the bald fact remaining that it is not materially raised by this drug, in these cases under the circumstances mentioned. More or less vigorous massage is useful, probably by increasing the venous, lymphatic, and tissue-serum movement.

Already the composition of the tissue-serum is notably altered. It is especially significant that it contains an excess of sodium chloride; is usually acid to phenolphthalein; and is deficient in viscosity. If nutritive elements are present in normal amounts

they are probably less available than in health, or the cells do not so readily appropriate them, for, certain it is that at this time there is a measurable decline in nutrition, particularly apparent in loss of reserve fats. The possibility of improving the character of this liquid by appropriate feeding lends peculiar importance to the diet at this time. The presence of an excess of chlorides in the tissue serum, together with the well known effects of sodium chloride in increasing edema, has led to the formulating of the so-called "salt-free" diet. While approving of giving this subject the most careful and favorable consideration, I wish here to enter an emphatic protest against dignifying the important process of adjusting the amount of table salt to the requirements and capacity of the body tissues by exalting it as a system of treatment. With the object in view of replacing the excess of sodium chloride by the like salt of lime, and possibly increasing the viscosity of the tissue serum, I am accustomed to give lime, preferably in the form of the lactophosphate, in fairly large doses, and with apparent benefit. The same results may be had by giving, in suitable quantities, milk, gelatine, and other lime-bearing foods. To my mind the question of how to maintain the mutual attraction between the tissue cells and tissue serum, and the viscosity of the latter, in order that this liquid, as it envelops the cells of the body, may move along with just sufficient velocity to allow a maximum amount of required nutritional cellular absorption, and of waste extrusion, is one, if not the most important and urgent, of the problems confronting us.

Reverting to the details of the diet at this time, it is clear that, because of the loss of reserve fats, and the use of the body proteids, as evidenced by the increased urea excretion and loss of weight, particular attention should be directed toward meeting, fully, the caloric requirements of the individual, and the directions for this should be definitely formulated by the physician. Until every vestige of tissue serum excess has been drained away, the intake of liquids should be well below that of excretion, as determined by actual weight and measure. With restored circulatory equilibrium the ingested liquids should approximate the standard which experimental study has proved to be most suitable for the patient. It is well, at this time to repeat the mercurial mass at more frequent intervals, and the saline may be given every morning, if the exigencies of the case requires. The rigidity of this plan of management may be lessened with precautionary oversight, but there should be a close adherence to the fundamental principles involved. These special measures should be continued for a sufficient time to allow as complete restoration of the circulatory balance as possible. This may be, in rare cases, about a month; usually at least six weeks are required; in some cases, especially those in which a recent infectious illness has been experienced, a much longer time will be necessary.

Between the stage of this malady which has been just considered and the terminal one is a wide gap and a long interval. During the intervening periods there will have been some in which the patient's condition is eminently satisfactory, the circumstances considered; others of relapses, disappointments, and distress. The management will have been one of increasing care and strictness, passing gradually through the steps intervening between those which have been mentioned and those which will now demand our attention.

In the stage to which I now refer the patient has passed through a prolonged period of great distress. There has been such respiratory distress as to prevent the patient assuming the recumbent posture, sleeping fitfully in his chair in a more or less erect and uncomfortable position. There have been a variety of uremic manifestations, such as headaches, wakefulness, muscular twitchings, visual scintillations, drowsiness, mental dullness and aberrations, etc. Retinal and other hemorrhages may have occurred. Occult edema has appeared, and gradually increased, with augmented distress, to the greatest tension, when, fitfully, the restraining barriers of intercellular tissue-serum attraction and areolar tissue resiliency gives way, and with notable relief from the distressing symptoms, dependent dropsy is an established fact. The patient is now in a present and visible danger; the management assumes an importance, not greater, but more acute. What shall it be?

Removal of the superfluous tissue serum is an essential first step. This is best accomplished by the use of elaterin. The method of procedure is important. During three days the diet should consist of thin gruels, cream and water soups, tea, coffee, water, and carbonated waters. The first and second days the total quantity should be about 1500 c.c. per day; during the third day the quantity should not exceed 1000 c.c., and the gruels and soups should be taken very sparingly or omitted. Every night, including the night preceding the first day, there should be taken 10 grains of mercurial mass, in two freshly-made pills of 5 grains each. The first following morning there should be taken an ounce of castor oil; on each of the other mornings there should be taken an efficient saline cathartic. Beginning with the fourth morning, give $\frac{1}{20}$ grain pure elaterin every hour for three doses; later $\frac{1}{10}$ grain every two hours until ten or twelve very free watery movements have been secured. This may require two or three days, during which time the patient should have no solid foods, and very little liquids. Later the standard diet, modified as may be required, should be gradually resumed. The total number of liquid stools will probably be from 15 to 20, and the quantity of tissue serum drained away, from 5 to 20 pounds. The filtered serum thus evacuated should be analyzed, and the results recorded. It is usually acid, straw or

amber colored, having a specific gravity of from 1005 to 1030, and heavily laden with chlorides. The odor is sometimes peculiarly offensive. Following the intestinal drain the flow of urine usually becomes very free; I have seen the day's excretion reach the enormous quantity of 6000 c.c., when previously it had been scanty. The siphonage thus started ordinarily continues as a free flow until the edema has completely disappeared; nevertheless, this action should be assiduously encouraged and stimulated, for example, by the use of infusion of active digitalis leaves, theocine, external warmth, the recumbent position, etc. During the entire course the intake of liquids should be well below the output. The advantages of this method of removing dropsical liquids lies, primarily, in the fact that they are selectively excreted by the intestinal and renal cells, ordinarily the albuminous and other useful nutritive materials largely remaining behind.

In some cases, from various causes, the method thus shortly outlined is impracticable. It will then be necessary to remove the serum directly from the subcutaneous tissues, preferably by means of Southey's tubes. The pointed stylet makes an opening through the skin mainly by spreading the tissues; the small tubes are tightly grasped by the elastic tissues, thus preventing leakage; closure promptly follows removal of the tubes, and with the employment of full antiseptic precautions, infection is almost unknown. Two tubes in each leg, one inside and the other outside, inserted just above the ankle, or at any other more available points, are usually sufficient. Rubber tubes of the smallest caliber, as soft rubber catheters, should be attached to the ferruled ends of the silver tubes and tied with ligatures, the ends of which may be used in retaining the tubes in place. In this manner the surface is kept dry, the draining tissue-serum being conveyed to suitable receptacles, thereby adding to the comfort of the patient and reducing to a minimum the liability of infection. The patient should assume a semirecumbent posture, preferably sitting in a chair, or lying in a specially prepared bed which insures an inclined plane for the body, with the feet in the most dependent portion. He should be made as comfortable as possible, inasmuch as much fortitude is required. The drainage should be continued until the edema has largely disappeared, and the flow reduced to an insignificant amount. Usually there may be removed in this manner from 10 to 30 pints in twenty-four hours, and from four to seven days of gradually decreasing flow will be required to complete the process. The advantages of this method lie in the directness of the attack and the certainty of results; the very obvious objection to it is that the tissue serum is drained off as a whole, including its albumin and other nutritive materials. Upon removal of the tubes a dry antiseptic powder should be used and an elastic bandage applied to the

feet and legs. The feet should be kept at a higher level than the hips. The small openings rapidly close under this management.

Removal of these large dropsical accumulations discloses an astounding degree of emaciation, although this may be anticipated with great exactitude from the moment when occult edema is detected. With complete exhaustion of the stored-up fats, and the patient's proteid tissues already heavily drawn upon, we are brought face to face with a very formidable situation, inasmuch as the continuation of this condition will lead to starvation acidosis, with all its distressing features. To meet this condition there will be required a most careful adjustment of the dietary, in the formulating of which close attention should be given to its every detail. The following may be considered as typical only, inasmuch as the individuality of the patient and his requirements must dictate the dietary:

	Grams.	Calories.
Breads of all kinds, a minimum of	124.0	496
Oatmeal, or other cereal, a minimum of	31.0	124
Rice, variously prepared, a minimum of	31.0	124
Potato, variously prepared a minimum of	62.0	248
Meat, fowl, or fish, lean, a minimum of	31.0	124
Meat, fat, a minimum of	31.0	279
Eggs, a minimum of	96.0	384
Sugar, a minimum of	15.5	139
Butter, a minimum of	15.5	155
Cream, 15 per cent., a minimum of	124.0	186
Milk, 3 per cent. cream, a minimum of	500.0	150
Cheese, a minimum of	15.5	162
Total		2571

To these there may be added, or to an equitable extent substituted for a portion, all kinds of succulent vegetables and fruits, properly prepared. The table salt should be limited to somewhat less than the secretory capacity of the patient's kidneys. The same should apply to the liquids taken; ordinarily from 1000 c.c. to 1500 c.c. is the proper quantity, but it should not exceed the output by the kidneys and intestines.

In conclusion, it is clearly impracticable to follow the various lines of management which should be pursued through the advancing stages to a fair or moderate symptomatic recovery; and quite impossible to do so through the deviousness of the downward path. Suffice it to say that some of the successes may well take rank among the marvels of medical achievement; and even in those, only too numerous, pursuing an unfavorable course, we may not infrequently feel assured that by giving our patients all the advantages of the methods and details of management which the present state of knowledge permits, with the measure of perception, tact, diligence, and fertility of resource which should be given them, their days have been lengthened and made more comfortable and useful.

BACILLUS DYSENTERIÆ RECOVERED FROM THE PERIPHERAL BLOOD AND STOOLS OF CASES IN PANAMA.

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AND
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(From the Board of Health Laboratory, Isthmian Canal Commission, Ancon Hospital, C. Z.)

The following cases are reported for several reasons: (1) To note the occurrence of Bacillus dysenteriæ in this region, the Canal Zone and the native village of La Chorrera, Republic of Panama. (2) The isolation of Bacillus dysenteriæ (Shiga strain) from the circulating blood in a fatal case of dysentery. (3) To emphasize the value of special media (Endo) in shortening the otherwise laborious technique of isolating Bacillus dysenteriæ from stools.

In their efforts to isolate the dysentery bacillus from stools and autopsy material many workers inoculate large numbers of agar plates from broth cultures and then endeavor to pick the desired colonies after a macroscopic and microscopic examination. The suspicious colonies are then usually inoculated into a nutrient medium containing glucose and litmus, all gas formers being rejected, the rest saved for further study. Sometimes the number of colonies thus studied runs into the hundreds. This entails many hours of work, which work may be done in almost as many minutes by the use of a differential medium at the start. Many differential media have been suggested and used[1] for the isolation of the typhoid bacillus, but little advantage seems to have been taken of this method in isolating the Bacillus dysenteriæ.

In our routine work of examining the stools and urine of typhoid convalescents for typhoid and paratyphoid bacilli we have used Endo's[2] medium, and on account of the several biological characteristics which the dysentery bacillus has in common with the typhoid bacillus, this medium immediately suggested itself to us as an excellent one for the isolation of the dysentery bacillus.[3] Neither the typhoid nor the dysentery bacillus ferments lactose, while many of the intestinal bacteria, especially Bacillus coli and its near relatives, as well as many representatives of the coccaceæ, ferment lactose.

In Endo's medium 10 grams of lactose and 1.8 c.c. of a 10 per cent. alcoholic solution of basic fuchsin are added to the liter and

[1] Pratt, Boston Med. and Surg. Jour., 1907, clvi, 744, 788, 813.
[2] Centralbl. f. Bakt, 1904, xxxv, 109.
[3] Proceedings Canal Zone Medical Association, August, 1909.

the medium then barely decolorized by the addition of a 10 per cent. aqueous solution of sodium sulphite.

According to Endo,[4] fuchsin apparently is composed of the acid salt rosanilin $C_{20}H_{19}N_3HCl$. Rosanilin is a colorless so-called leucobase which, with various acids, such as lactic acid, acid salts, etc., forms a red dye. The acid component of the red rosanilin salt is easily reduced by sodium sulphite. The decolorized rosanilin combines with the acid produced by the colon bacilli and regains its red color.

This gives a red color to a colony which splits lactose with the formation of acid. In sharp contrast with the red Bacillus coli colonies, the typhoid, paratyphoid, and dysentery colonies which do not act on the lactose come out small, colorless, and translucent, like small drops of dew. The length of the period of incubation varies from twelve to forty-eight hours, according to the nicety of adjustment of the reduction with the sodium sulphite. There are several other microörganisms which present a similar appearance on this medium, as, for instance, Pseudomonas pyocyanea or the paracolon bacillus, but their number is usually so small that they do not interfere seriously with this method.

In our routine work all suspicious colonies are inoculated into broth; this is incubated for twenty-four hours, and then subinoculations are made on agar slant, potato, in litmus milk, Dunham's, and into each of the following semisolid media: Glucose, lactose, dulcite, saccharose, maltose, mannite, dextrin, and galactose. The semisolid medium is used on account of its greater sensitiveness in exhibiting gas formation and motility. Agglutination tests are made with a saline emulsion of the growth from the agar slant and Bacillus dysenteriæ immune serum.

With the use of the Endo plates the examination of a large number of Bacillus coli-like colonies is also obviated, as the original material is immediately spread on the plates without the previous inoculation of broth. When broth is inoculated, Bacillus coli multiplies much more rapidly than Bacillus dysenteriæ and increases the difficulty of detecting and isolating the latter.

The first patient from whose stool we isolated Bacillus dysenteriæ was a white American working in the laboratory. The source of infection is doubtful, for the patient lived at Ancon, where there has been no epidemic gastro-intestinal disease since "El Mayo"[5] in 1905. He may have become infected from an autopsy held on July 29, 1909, a few days before the onset of his attack.

The autopsy was one of chronic nephritis with ulcerative colitis. Cultures from the gut, however, contained chiefly Bacillus coli and

[4] Loc cit.

[5] "El Mayo" is the local name for an epidemic diarrheal disease which appears in Panama at the beginning of the rainy season.

streptococci. No Bacillus dysenteriæ could be detected. Another possible source of infection was one of enterocolitis in an American child, aged two years, born in the United States. The child had been embalmed by the patient whose case is reported here, and opportunities for infection occurred June 23 and June 29, four to five weeks before the onset of the disease in question.

He was sick one day before admission to the ward. The second day in the ward he had fifteen movements, the third day forty, and from then on a gradually decreasing number. These movements were fluid and contained much mucus, pus, and blood. He ran a slight continued fever, the highest point reached being 100° F. On the seventh day of his illness a specimen of his stool was sent to the laboratory. This was stroked on Endo plates, and the resulting growth showed many typhoid-like colonies. Fifteen of these were planted in glucose semisolid. Some of them were Pseudomonas pyocyanea but three colonies on subcultivation in thirteen media had the cultural characteristics of Bacillus dysenteriæ. These three colonies were all agglutinated with the "Y" immune serum in a dilution of one to six hundred in less than two hours, and by the Flexner and the Shiga immune sera in lower dilutions. This was a severe and typical case of bacillary dysentery due to the "Y" bacillus and apparently was a sporadic case.

The second case is one which has several peculiar features. The patient, a negro and Zone charity case, entered the hospital on May 13, 1910. He had been sick for six days when he entered the hospital and gave a history of abdominal pain and of passing blood and mucus. The physical examination showed marked tenderness over the colon, few rales in the lungs, enlarged glands, heavily coated tongue, weak heart sounds, slight injection of the conjunctivæ, enlarged liver and spleen. He had a leukocyte count of 27,500. All his movements were fluid, containing much blood and pus. On the first, fourth, and fifth days after admission he had severe hemorrhages from the bowels. The largest number of bowel movements recorded on any one day was eleven. The highest point his temperature reached was 101° F. On the night of his admission he had a severe hemorrhage from the bowel, and a blood culture was taken the following morning. On account of this loss of blood, only a small amount was taken (about 4 c.c.), and this was inoculated in bile-glycerin-peptone solution, not being inoculated in oxalated broth as is usually done. This bile-glycerin-peptone was incubated for twenty-four hours and then agar plates made. At the end of twenty-four hours' incubation these showed many colonies which were smaller and more transparent than typhoid colonies. Agglutination tests were made with these and typhoid immune serum, paratyphoid A, immune serum, paratyphoid B immune serum in various dilutions. In none of these did agglutination occur.

Several colonies were now taken from the agar plates and grown in broth for twenty-four hours and these subinoculated on agar slant, potato, in litmus milk, in Dunham's medium, and into each of the following semisolid media: Glucose, lactose, dulcite, saccharose, maltose, mannite, dextrin, and galactose. On these media each culture showed the cultural characteristics of Bacillus dysenteriæ (Shiga strain) with the exception that the litmus milk did not become alkaline after prolonged incubation. Agglutination tests were carried out with some fresh therapeutic antidysenteric serum which we had just received from Mulford. This serum is a combination of two sera, Shiga and Flexner. Each component will agglutinate the dysentery bacillus from which it was derived in dilutions of one to one thousand, and other varieties in a dilution of one to five hundred. Testing our organism with this serum, it agglutinated in dilutions of one to one thousand and lower in less than two hours, and in a dilution of one to two thousand in two hours. As a matter of control, agglutination tests were carried out with this serum and typhoid, paratyphoid A, paratyphoid B, the colon bacillus, and several other organisms of this group, in every instance with negative results.

The patient died on the tenth day of the disease. The autopsy was performed by Dr. H. C. Clark. From the autopsy findings the following is quoted: "Very slight increase in peritoneal fluid. All mesenteric, mesocolic, and periportal glands are noticeably enlarged, the ones about the cecum showing the greatest change. No visible change in the peritoneal covering of the intestines. . . . When the large bowel was opened there was found to be a very diffuse diphtheritic inflammatory process from the rectum to the ileocecal valve. In the cecum and ascending colon it had become almost gangrenous, while throughout the rest of the gut a bright red, coarsely granular, inflammatory process with a diphtheritic exudate was found."

Hence we have a case of acute dysentery authenticated by autopsy findings in which the dysentery bacillus was recovered from the blood stream four days before death, proving that Bacillus dysenteriæ may be found in the circulating blood in spite of statements to the contrary by several authorities.

The only detail in which this bacillus differs from the Shiga bacillus of classical description is in its effect upon ordinary litmus milk. It turns this a lilac color, which is a sign of slight acid reaction and remains thus permanently. Torrey[6] states: "Several cultures belonging in Group I, which when first isolated were entirely typical in the effect on litmus milk, did not produce, about six months later, a marked alkaline reaction. After returning to amphoteric there was no change to alkalinity, but, if anything, the

[6] Jour. of Exper. Med., 1905, vii, 372.

medium appeared slightly more acid than the control after three weeks' incubation."

Again, our milk from the hospital dairy, although neutral to litmus, is almost invariably as strongly acid as may be used, requiring from 15 to 17 c.c. of decinormal sodium hydroxide per liter to neutralize it, using phenolthalein as an indicator.

Jordan[7] makes the positive statement that the dysentery bacillus is not found in the blood stream.

Castellani and Chalmers[8] state that the dysentery bacillus has been recovered from the blood stream by Rosenthal and Markwald, but give no reference.

The third case was that of an infant, aged eight months, seen during an investigation of a reported outbreak of diarrheal disease at the native village of La Chorrera, August 22, 1910, about twenty-five miles from Panama. The parents gave a history of the child having dysentery. A Löffler blood serum slant was inoculated with swab material from the rectum. Two days later, when the culture reached the laboratory, a saline emulsion of the growth on this slant was made and spread on Endo plates. From these plates several organisms were recovered which conformed culturally with the "Y" organism of Hiss and Russell. These agglutinated with Mulford's anti-dysenteric serum in a dilution of one to one thousand in one-half hour.

To summarize: (1) By the use of a differential medium (Endo's) we have been able to isolate Bacillus dysenteriæ, the "Y" type, from two sporadic cases of dysentery, one a white American, an inhabitant of Ancon, Canal Zone, the other an infant living in and native of the small village of La Chorrera in the Republic of Panama.

2. We have recovered from the circulating blood of a fatal case of dysentery, in our routine blood culture work, Bacillus dysenteriæ, one which agglutinates with antidysenteric serum in a dilution of one to two thousand and is culturally of the Shiga type.

NOTE ON THE FAVORABLE INFLUENCE OF QUININE AND UREA HYDROCHLORIDE IN LARGE DOSES UNDER THE SKIN IN THE TREATMENT OF ACUTE PNEUMONIA, LOBAR AND LOBULAR.[1]

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There is a long-standing tradition that quinine given early will abort an attack of lobar pneumonia. In an early experience

[7] General Bacteriology, p. 285. [8] Manual of Tropical Med., 1910, New York.

[1] Read before the Association of American Physicians at Atlantic City, May 1911.

of the writer's, 60 grains of quinine sulphate given in error in a period of five hours, beginning two hours after the initial chill, apparently acted in this manner. Galbraith's revival of the treatment of pneumonia by quinine in massive doses (1904) led the writer to employ it at the Philadelphia General Hospital and at the Hospital of the Jefferson Medical College; soon, however, substituting hypodermic for gastric administration (as advised by Aufrecht, Petzold, and Henry),[2] and choosing the most active salt of quinine, namely, the double hydrochloride of quinine and urea, with which he has had such favorable experience in the treatment of malaria.[3] The initial dose (regulated somewhat by the height of the temperature) is 1 gram to 1.6 grams (15 to 25 grains). This is followed in three or four hours by a second injection, and perhaps by a third and even fourth injection, at some time within the first twenty-four hours, according to results. The same plan is pursued on the second day of treatment and on the third day, if necessary. Usually from 6 to 10 grams are given in from forty-eight to sixty hours. After that smaller doses (5 to 10 grains—0.3 to 0.6 gram daily) are sometimes continued by the mouth.

Cinchonism does not develop. Temperature and pulse-rate fall gradually and proportionately, and respiration more rapidly, with a tendency to restoration of the normal pulse-respiration ratio. Blood pressure may at first decline with temperature and pulse frequency, but soon returns to the former or a higher level; often it remains stationary or increases. The complete clinical picture, so far as regards the rational symptoms, objective and subjective, is thus favorably changed. The patient professes comfort; the pulse is full and strong, of moderate frequency and good tension; respiration is astonishingly easy, even when the rate is not markedly altered; the cough is greatly diminished; and delirium, if present, is abated, or may even cease. Crisis does not occur. Termination is by lysis at about the ordinary time, five to twelve days. The only critical phenomenon observed, and this but rarely and in slight degree, is perspiration. Usually there is some mild sweating with the early fall of temperature and respiration.

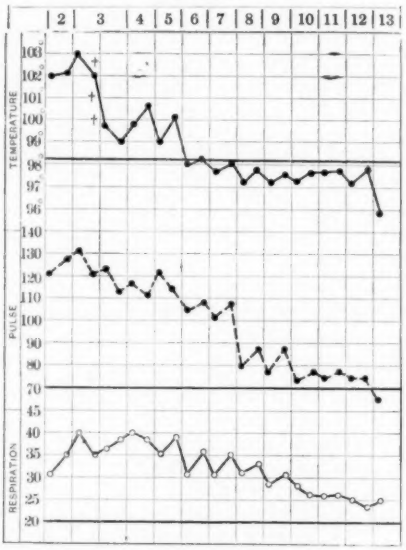
Percussion and auscultation signs, however, are uninfluenced. Even when the case is seen and treated comparatively early, dulness and bronchial breathing increase. The rales of resolution appear at the usual time, but not earlier. Involvement of new areas may take place during treatment, with return of symptoms, necessitating new injections. Pneumococcic empyema has occurred. The structural pathological processes, therefore, would appear to evolve

[2] Remarks on the Treatment of Pneumonia, by F. P. Henry, Phila. Med. Jour., February 14, 1903.

[3] Amer. Jour. Med. Sci., September, 1908.

in the customary manner, unmodified by the treatment, which is apparently not germicidal. Systematic and accurate quantitative observation of urinary chlorides is lacking, but a few approximations show no apparent deviation from the ordinary rule. Leukocytic studies as yet show nothing definite. A slight increase, not especially affecting any one variety, is the most common observation.

CHART I.*



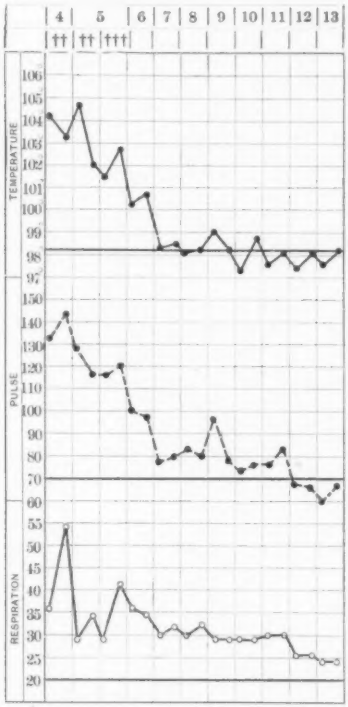
* The numerals at the top of the chart show the day of disease.

Abstract of Case, Chart I. Observations *at first* every four hours; then twice daily. *Acute lobar pneumonia; severe; left apex; alcoholic.* R. M., male, aged sixty years; laborer; colored. Chill; herpes; no jaundice; no vomiting; no delirium; slight cyanosis. Blood culture shows pneumococci. White blood cells, 24,000. †Three injections, 1 gram each; total quantity, 3 grams during twenty hours. First injection on third day; last injection on third day. White blood cells, 32,000 (increase 8000). Duration from chill to resolution, twelve days. Complication, pleurisy. Result, recovery.

The most striking results of the large doses of quinine are thus functional; and since the most significant features are the relief of respiration and the maintenance of normal cardiac vigor and blood pressure, it seems logical to infer that the effect is chemical and antitoxic. This view is further borne out by the absence of quinine intoxication, suggesting a mutual neutralization of disease-poison, and drug. It may be, however, that the antitoxic action is indirect; or that the drug acts, in part at least, as a direct stimulant to the autonomic cardio-respiratory centres. Experimental obser-

vations on this point are desirable, but the writer has thus far failed to arouse a sufficiently lively interest in any trained experimentalist.

CHART II.*



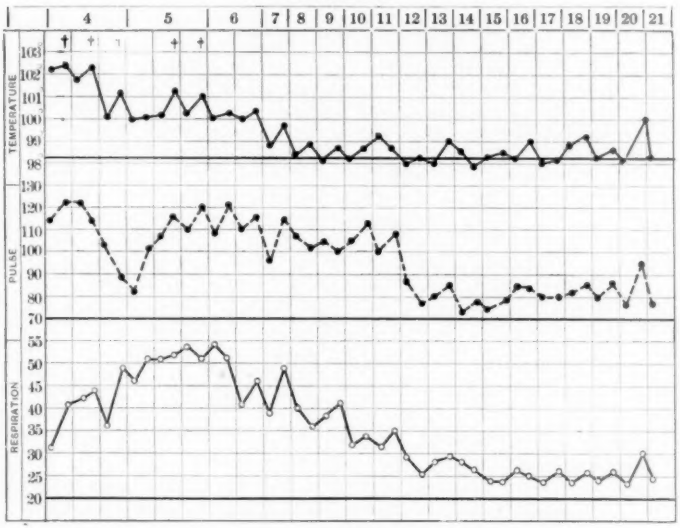
* The numerals at the top of the chart show the day of disease.

Abstract of Case, Chart II. Observations *at first* every fourth hour, then twice daily. *Acute lobar pneumonia; severe; right lower lobe.* S. S., female, aged fourteen years. Pneumococci in sputum; chill; no vomiting; no herpes; no cyanosis; no delirium. White blood cells, 14,000. †Seven injections, 0.5 gram each; total quantity, 3.5 grams in twenty-eight hours. First injection on fourth day; last injection on fifth day. White blood cells, 15,000 (increase 1000). Duration from chill to resolution, thirteen days. Complication, pleurisy. Result, recovery.

The total number of cases of acute lobar pneumonia thus treated and observed with sufficient accuracy for purposes of record was 87, with 16 deaths. Nearly all the deaths, however, occurred at the Philadelphia General Hospital, where the expected mortality of the unfavorable class of cases received is from 25 to 50 per cent., varying with the year. A much larger number of cases than that mentioned was treated by this method in the course of the

seven years that it has been carried out in the writer's hospital services, and more recently in private and consultation practice, with a total mortality of 12 per cent. (23 deaths in 192 cases). If alcoholic cases, terminal infections, pneumonia of the aged, patients over fifty years of age, and patients of all ages received on or after the third day of the disease, were excluded, the mor-

CHART III.*



*The numerals at the top of the chart show the day of disease.

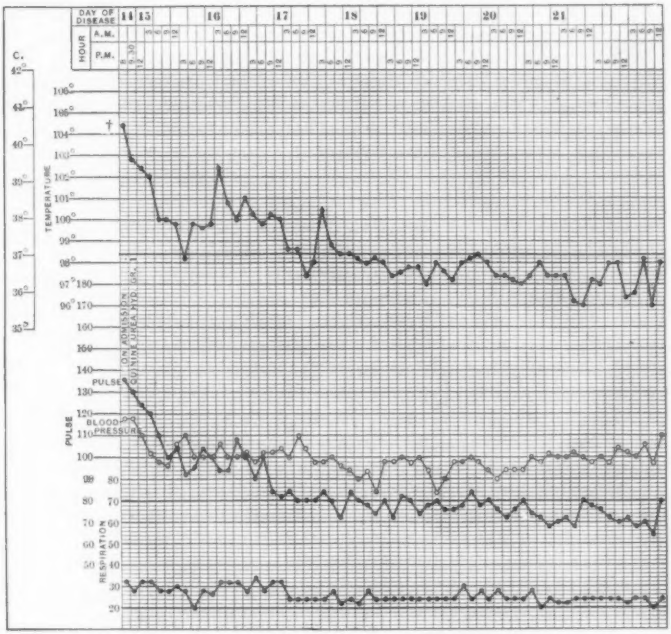
Abstract of Case, Chart III. Obervations *at first* every fourth hour; then twice daily. *Acute lobar pneumonia; severe; right lung; left lower lobe.* S. St. L., male, aged twenty-eight years; seaman; black; not alcoholic; no venereal disease. Chill; cyanosis; delirium; no vomiting; no herpes; no jaundice. Pneumococci in sputum. White blood cells, 12,000. Urine contains pus, hyaline, and granular casts; chlorides diminished. †Five injections, 1 gram each; total quantity, 5 grams in sixty hours. First injection on fourth day; last injection on fifth day; fall of temperature after fourth injection. White blood cells, 20,000 (increase of 8000). Delirium abated; duration from chill to resolution twenty days. Complication, pleurisy. Result, recovery. It will be noted in this case that respiration continued to increase until after the fourth injection had been given. This was coincident with extension of the process in the right lung. Blood pressure, which is not shown upon the chart, was, however, favorably influenced from the beginning.

tality would be inconsiderable; but to exclude all of these cases would be to exclude also a large proportion of the recoveries. Even in fatal cases the patient's comfort was notably promoted.

While these studies were in progress, other cases were admitted to the writer's services and recovered without any special medication; the quinine treatment being reserved for cases in which decisive therapeutic intervention seemed necessary. Inclusion of the milder

cases among those treated would have lessened the mortality percentage. In the earlier observations patients admitted very late and in bad condition were not given quinine, and recovered or died under other plans of treatment. In the later experience, such patients also received the injections and usually with noticeably

CHART IV



Abstract of Case, Chart IV. Observations every third hour. *Acute pleuropneumonia (lobular), quite severe.* E. L., female, aged twenty-three years. Left upper and lower lobes; right middle lobe. Cyanosis. Not alcoholic; no venereal disease; no chill; no delirium; no vomiting; no herpes; no jaundice. Sputum contains a few gram-positive diplococci, many streptococci and staphylococci. Admitted fourteenth day. Blood pressure below pulse frequency. †One injection, 1 gram. Prompt fall of temperature, pulse, and blood pressure. Subsequent rise of blood pressure beyond pulse frequency. White blood cells, 15,000. Duration to complete resolution twenty-four days (ten days after injection). Result, recovery.

good results. In no case was a bad result observed that could be attributed to the drug. While the statistics of recovery suffered, many individuals got well that otherwise might have perished.

In addition to the use of the quinine salt, fresh air, water, and all other necessary measures of good nursing were provided; and such agents as strychnine, digitalis, alcohol, camphor, opium, cocaine, epinephrin, musk, and alkaline diuretics were administered when

symptomatically indicated. Special attention was paid to the consonance of pulse rate in beats per minute with systolic blood pressure, measured in millimeters of mercury, as advised by G. A. Gibson,[4] of Edinburgh, and by Hare;[5] excess of the number representing frequency over that representing pressure thus measured, being met by appropriate medication. In a number of cases saline infusion was also used, and in some of these, oxygen as well; the latter measure chiefly as a palliative in the fatal cases, as in those cases which ran a favorable course it did not often seem to be necessary. In the cases treated during the last two years, sodium bicarbonate or ammonium compounds were given in sufficient quantity to keep the urine alkaline throughout the course of the attack, and this seems to have been of benefit. Following Galbraith's plan, tincture of ferric chloride was given when the quinine was withdrawn. Lobular pneumonia was influenced favorably in a similar manner to lobar pneumonia.

Four charts are selected for reproduction as illustrative of different types of cases.

In *making the injection*, the following precautions, published by the writer in 1887, and several times since, must be observed; otherwise there may be cellulitis, slough, or abscess. The syringe is filled with a 50 per cent. solution of the quinine and urea salt in sterilized water; and the needle is inserted deeply, through skin previously painted with tincture of iodine, into a muscle. The syringe is emptied thoroughly, so that solution does not drop upon the skin when the needle is withdrawn. The point of puncture is sealed with iodoform-collodion. Thousands of injections have been made in this manner without ill-result of any kind.

BRONZED DIABETES. REPORT OF A CASE WITH SPECIAL REFERENCE TO THE INVOLVEMENT OF THE PANCREAS IN DIABETES.

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and

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The following case when first seen was readily diagnosticated as an example of that rare symptom complex or combination of diseases picturesquely named by the French "Bronzed Diabetes."

[4] Edinburgh Med. Jour., January, 1908, lxv, 22; G. A. Gordon, Ibid., January, 1910, n. s. iv, p. 37.

[5] Therap. Gaz., 1910, xxxiv, 397.

The patient was closely followed for an extended period of time, and in this way provided an excellent subject for the study of the various manifestations of the disease. Our clinical and pathological observations are therefore of considerable value to the literature upon a subject in which theoretical considerations have generally overbalanced the account both of the clinical course and of the postmortem abnormalities. A careful examination of the sections of this patient's pancreas stimulated one of us to further study into the intricate connection between this organ and diabetes, and led to some tentative conclusions at variance with what is generally accepted.

The case was as follows: A male, aged fifty-five years, a timber merchant, first came under observation in March, 1908, on account of weakness, loss of weight, irritability, and increased frequency of urination. There was also slightly increased thirst. For several months he had been constantly testing his urine for glucose, and was much depressed when any was demonstrated. Increased frequency of micturition was first noticed six years before while traveling in Spain. He gained weight for several years, and until four years ago weighed 247 pounds. At that time he began to feel lazy and tired. Two years ago, when traveling up the Nile, eating considerable sweets and drinking 1 or 2 pints of champagne daily, the patient again noted increased frequency of urination and increased amount of urine, especially at night, and glycosuria was demonstrated. Since January 1 of this year his diet was rather strict. The amount of urine varied from 50 to 75 ounces daily, and with Hayne's test 3 to 4 drops produced a reduction. He has been upon a more or less strict antidiabetic diet ever since, with intervals of disappearance of sugar from the urine. For the last three years he has been annoyed by cough, expectoration, slight, gradually increasing dyspnea, and cold hands and feet. He was told by a physician that he had a "spot on his lungs."

Family History. Married; no children; wife never had miscarriages; father died suddenly, aged fifty years, of "rheumatism and heart disease;" mother died, aged sixty-four years, of "Bright's disease;" grandfather died, aged ninety-eight years, of "diabetes." One younger brother is subject to "muscular rheumatism."

Habits. He used alcohol very moderately until five or six years ago. Since then he has taken a pint of wine and one or two whiskies daily. He uses tobacco—6 cigars, an occasional pipe, and 10 or 12 cigarettes daily. He has been a large eater for the last ten years. He is fond of sweets, but rarely eats them to excess.

Past History. Venereal diseases denied. No evidence of syphilis. "Sunstroke" twenty-five years ago (during very hot weather), fell suddenly from moving car, struck back of head, lost memory for few days; "neurasthenia" for one year afterward. He did not

feel perfectly well after this for six or seven years. He is not subject to headaches. Mild attack of gout twenty years ago. Subject to occasional attacks of "biliousness," and twice vomited large quantities of "partly digested blood." Hemorrhoids never noted. He has traveled extensively in hot countries, but has never had malaria. Consulted dentist frequently during last ten years for trouble with his gums. Has been taking veronal for insomnia. He has never taken arsenic or silver, so far as he knows, nor has he been subject to any affection of the skin.

Physical Examination. Height, 6 feet 1 inch; weight, 200 pounds; nutrition fair, abdomen prominent. Color of face deep brown and somewhat cyanotic. Mucous membrane of mouth brownish blue in color. Tongue dry, red, fissured, and clean. Gums bled easily. Pharynx dry and congested. Teeth irregular and decayed. Breath, slightly sweetish odor. Wrists, fingers, and hands brownish-blue color, palms reddish. The legs and feet were pale yellowish brown, cold, and cyanotic, and the veins rather prominent. Skin of the body was pale yellowish brown, soft, smooth, delicate, and distinctly dark for a blond man. The superficial and deep reflexes were normal.

Heart. Dulness slightly increased both to left and right. The aortic second sound was accentuated. There were no murmurs.

Lungs. Nothing abnormal detected.

Spleen. Enlarged, easily palpable at costal margin.

Liver. Upper border in fourth space in right midclavicular line; lower border hard but smooth, palpated three fingers' breadth below costal margin in right midclavicular line.

No special enlargement of abdominal veins and no ascites. No glandular enlargement.

Urine. 3600 c.c. in twenty-four hours. It contained 18.5 grams of sugar, no acetone, a slight trace of albumin, and occasional casts.

Progress of Case. During the next four months the sugar in the urine from time to time disappeared altogether, and the amount of urine varied between 1500 c.c. and 2900 c.c. On one occasion the quantity of urine reached 4400 c.c. in twenty-four hours and contained 33.75 grams sugar.

November, 1908. The color, particularly of the face and dorsum of hands, had deepened. In the axillæ and around the genitals there was considerable dark pigmentation. This was not patchy, nor was there any leukoderma. There was a more or less sharply defined line of demarcation between the neck and wrists, and the adjoining body surface. The margin of pigmentation of the dorsum of the feet showed only a gradual transition. The palms were of a reddish blue without any brown tint. There was no ascites or edema. There was a short systolic murmur at the apex, but no increase of the cardiac enlargement. The gums were still markedly swollen and bled very readily, although they

had been thoroughly treated by a dentist. The temperature always remained normal or subnormal.

November 10, 1908, to January 25, 1909. Urine on an average amounted to 3500 c.c. per day, but varied between 1550 c.c. and 6800 c.c. The amount of sugar varied between 340 grams in twenty-four hours to as low as 4 grams. On only one occasion, no sugar was demonstrated. Acetone was almost constantly present. A trace of albumin and casts were also usually found.

Urinalysis.

	November 11, 1908.	January 22, 1909.
Amount	3360 c.c.	6505 c.c.
Specific gravity	1025	1011
Albumin	0	0
Indican	0	
Sugar	3.7 per cent.	0.8 per cent.
Total	124.5	48.6 g.
Acetone—		
Diacetic acid	0.318 gram acetone	0
Beta-oxybutyric acid	0.47 gram	0
Total nitrogen	26.10	14.62
Gross urea nitrogen	19.64 = 75.3 per cent.	10.80 75.4 per cent.
Net urea nitrogen	18.00 = 69.0 per cent.	9.88 69.0 per cent.
Ammonia nitrogen	1.64 = 6.3 per cent.	0.917 6.4 per cent.
Kreatinin nitrogen	0.725	0.420
Kreatin nitrogen	0.07	0.206
Uric acid nitrogen	0.425	0.114
Rest nitrogen	5.24 = 20.1 per cent.	3.08 = 21.1 per cent.
		January 21, milk day.
Total food: carbohydrate, 50 grams;		Total food: carbohydrate, 55 grams;
Fat, 300 grams; protein, 150 grams		Fat, 50 grams; protein, 40 grams

During this period he suffered from insomnia and attacks of facial neuralgia. In December, 1908, edema of the legs and ascites gradually developed.

April, 1909. Coughed up about a pint of blood, dark at first, then bright red. Ascites marked. No change in lungs, heart, liver, or spleen. Urine on an average contained 3 to 8 grains sugar to the ounce, and always some acetone and diacetic acid. The bronzing of the skin had become much more marked.

May, 1909. Developed a phlebitis of left saphenous vein which gradually subsided. Sciatica in both legs had also become very troublesome. There was also at this time periarthritic and arthritic swelling and tenderness of the right shoulder, hips, knees, and ankles. Upon a low carbohydrate and low protein diet, poor in salt, and with the help of free catharsis every few days, the edema and ascites gradually diminished.

December, 1909. Extremely edematous, abdomen very prominent from ascites. Heart considerably dilated and with long musical systolic murmur in the apex region. Blood pressure, 130. Bronzing of the skin much the same, but slightly more leaden in color.

Blood: Hemoglobin, 97 per cent., red blood cells, 4,760,000. White blood cells, 8900. Polymorphonuclears, 47 per cent.

Urine: (December 15) 1600 c.c. in twenty-four hours contained 109 grams sugar. Temperature always normal or subnormal.

January, 1910. Improved considerably with rest and dieting.

April 8, 1910. Ascites very marked again. Became incontinent of urine and feces. Urine contained pus, blood, and a considerable quantity of albumin and casts. The sugar content was 4.6 per cent. with no accompanying acetone bodies.

April 10, 1910. Died comatose.

The *autopsy* on this case was conducted six hours after death. Development and nutrition were fair. There was slight edema of the feet and marked protrusion of the abdomen from ascites. The skin showed a general faint brownish discoloration especially obvious on the back of the hands, the axillæ, the genitals, and the face, in which situations it also had a somewhat bluish tinge; and was associated with a considerable roughening and scaly appearance. The mucous membrane of the mouth was a faintly yellow color, as if from jaundice. There were no other skin lesions and no enlargement of the superficial lymphatic glands. The left pleural cavity contained about two pints of clear, slightly blood-tinged fluid. The right pleura was universally adherent.

The *lungs* were grayish in color, edematous, and congested, the lower lobe on the left side being somewhat collapsed.

The *heart* was slightly dilated and the myocardium, particularly of the left ventricle, somewhat atrophied and that of the right side considerably infiltrated by fat. The heart muscle was dark brown in color and very friable. The mitral valve admitted three fingers and the tricuspid five. There was slight thickening of the aortic and mitral orifices, but no endocarditis. The coronary arteries were considerably sclerotic near their orifices and the aorta was markedly atheromatous.

There was no smooth atrophy of the base of the tongue and no important change in the esophagus.

The *abdominal cavity* contained about 8 quarts of a yellowish, slightly turbid fluid. This was found to contain a small number of pus cells and a culture of staphylococcus albus.

The intestines were extremely distended and very edematous. The peritoneum was somewhat thickened, and on its surface were scanty patches of fibrinous exudate.

The *liver* was enlarged and showed coarse granulations on the surface and in its interior. It was dark brown in color, particularly in the parenchymatous islets. The fibrous tissue intersecting these islets was in considerable amount, dense, and congested. The gall-bladder was slightly dilated, its walls thin, and it contained no stones. The bile ducts were pervious throughout.

The *pancreas* was very small, densely embedded in fat so that

it could not be shelled out. It was extensively replaced by fibrous tissue, particularly marked in the middle of the body, where relatively little pancreatic tissue remained. The pancreatic lobules and to a less extent the intersecting fibrous tissue were dark rusty brown in color. No stones were found in the pancreatic duct.

The *kidneys* were slightly enlarged and showed a condition of cloudy swelling, but practically no chronic nephritis. They were yellowish brown in color, evidently also the seat of some pigmentation. In the cortex of both kidneys there were several small pyogenic abscesses, and the pelves of both kidneys were inflamed and contained a small amount of thin purulent material.

The *urinary bladder* was slightly dilated and was filled with a thin pus. Its walls were slightly thickened and its lining membrane inflamed and showed numerous hemorrhages.

The *lymphatic glands* in the abdomen showed no special enlargement, but on section were reddish brown in color, as if pigmented like the other organs.

The *brain* was very edematous. The vessels at the base, however, were only slightly atheromatous. With these exceptions there were no obvious gross lesions in any part of the brain.

Microscopic Examination. The skin in its deeper layer was the seat of a considerable deposit of granular yellow pigment, which for the most part gave the reaction of hemosiderin. The true skin was slightly atrophied and the stratum corneum considerably thickened. In the subcutaneous tissues no inflammatory condition could be observed.

The liver showed a condition of old-standing cirrhosis. The fibrous-tissue strands were well-defined, densely fibrous, and not particularly broad. The liver-cell masses were also sharply outlined and the liver cells had an irregular trabecular arrangement. The deposit of pigment in the liver was very extensive. It was chiefly massed in the liver cells and in slightly greater amount toward the periphery of the parenchymatous islets. In the individual liver cells the pigment was aggregated especially in the centre of the cell or toward the middle of the trabecula. The pigment was composed of small granules of more or less uniform size, bright yellow in color, and gave rapidly the iron reaction of hemosiderin. Some of the pigment granules, however, failed to give this reaction, thus resembling the hemofuscin described by von Recklinghausen. The pigment was not deposited in especially degenerate cells, and was in relatively small amount in the fibrous-tissue tracts. It was found in the lining cells of bile ducts, but practically no free pigment was contained in their lumen. The lymphatics in the fibrous areas in the liver commonly contained heavily pigmented mononucleated cells.

In the larger vessels in the portal spaces there were generally to be found a few isolated small granules of pigment among the red

blood corpuscles. These free granules in the bloodvessels were not in very large amount, and their presence in this situation did not appear to be the result of any artefact. Although it seems as if these granules were formed in the blood and secondarily deposited in the tissues, yet it is possible that mechanical postmortem influences, or a discharge of granules into the blood from the tissue cells may have been responsible for the appearance of pigment in the bloodvessels.

The spleen was in a condition of advanced venous stasis. The intersinus pulp cells were also somewhat hyperplastic, and the interior of the venous sinuses was frequently filled with mononucleated cells, evidently the result of some reactive process. Pigmentation in the spleen was relatively small in amount, although the cells lining the sinuses and in the intersinus tissue could commonly be seen containing small granules of yellow pigment.

The abdominal lymph glands showed slight hyperplasia of the lymph cells, but no necrosis or fibrous-tissue formation. As in the spleen, mononucleated cells were fairly frequently observed to contain granules of iron pigment.

The intestines in their submucous layer were considerably thickened by chronic inflammatory change. The mucosa was considerably atrophic. In the subepithelial tissues there was a particularly large number of small eosinophile cells. All of these changes, however, are not peculiar to the disease and may be found in any case of advanced liver cirrhosis.

The kidneys presented no evidence of chronic nephritis. The glomeruli and convoluted tubules were well preserved. Only a very small amount of pigment was found in the convoluted tubules and in the intertubular connective tissue.

The heart muscle cells were considerably atrophied, and the majority were loaded with the same granular pigment, chiefly hemosiderin, which was found in other organs.

The thyroid showed the usual spaces filled with colloid. Most of these spaces were comparatively small and some showed slight hyperplasia of the lining cells. In this situation also there was a very considerable amount of pigment in the cells lining the spaces and a small amount also among the colloid material.

The lungs showed chronic congestion and edema and only a very slight degree of pigmentation.

The brain in the cerebral cortex and in the region of the medulla showed no special histological change except slight edema. The nerve cells in the medulla occasionally contained a small amount of the same pigment found in the other organs, but did not appear in any way degenerated.

The pancreas was very extensively replaced by inflammatory tissue and by fat. The vessels in the interior of the organ showed no special change, and the ducts, although catarrhal, were not

dilated or obliterated by fibrous tissue. The parenchyma seemed to have been largely destroyed, but the portions which persisted among the inflammatory tissue were isolated as small rounded groups of acini (Fig. 1). Indeed, at first sight, all that seemed to have been spared were islands of Langerhans. The majority of these pancreatic remnants, however, were obviously acinous tissue, yet many also were definite islands of Langerhans. These latter, indeed appeared to be in considerable number, and many of them were well preserved. For the most part, they were larger

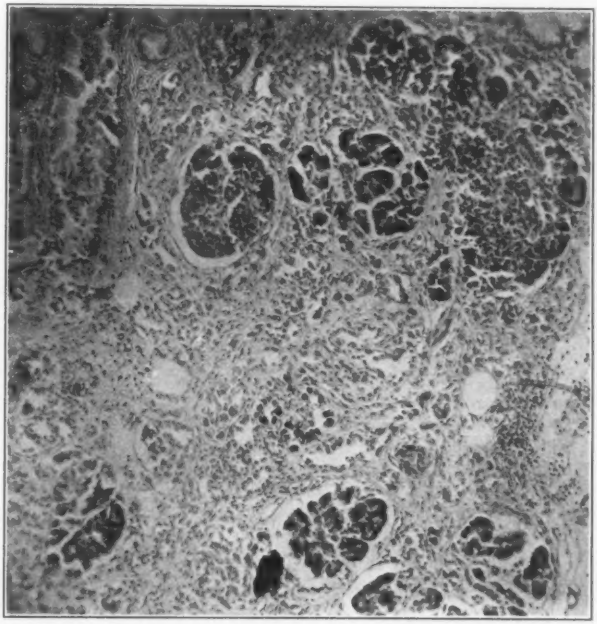

FIG. 1.—Pancreas from a case of bronzed diabetes, showing persistence of small remnants of pancreas tissue, many of which, although definitely acini, might be mistaken for islands. × 150.

than normal, although their number probably was less. In many places there were clumps of cells where it was almost impossible to differentiate between acinous and island tissue (Fig. 2). Isolated groups of acini seemed to become catarrhal, their cells became smaller, until structures apparently indistinguishable from islands were produced.

These transition figures in the pancreas, although they can only be accepted with some reservations, are particularly interesting, and are perhaps, sufficiently important to warrant a short digression into the morphology of the pancreas and its relation to diabetes.

The islands of Langerhans since their discovery in 1869, have provided a source of very varied discussion and their function is still uncertain. Numerous elaborate works on this subject have recently appeared, and most of them, Dewitt's,[1] for example, contain a very complete review of the literature. In these works

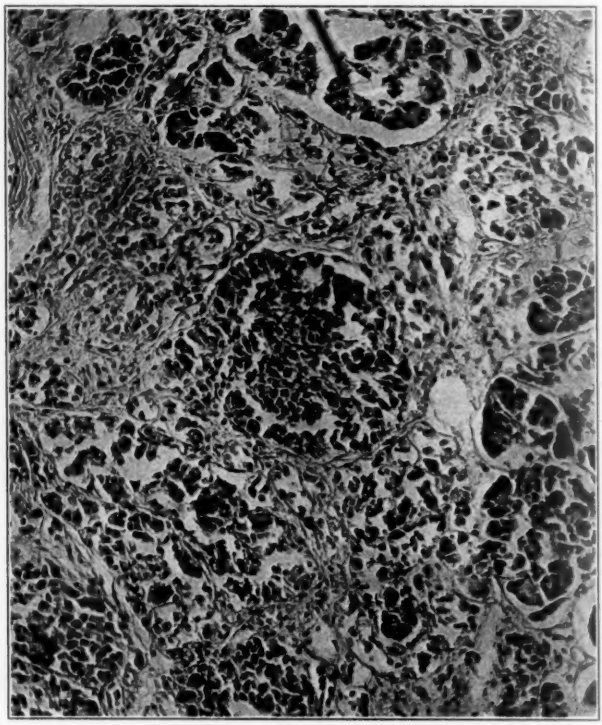

FIG. 2.—Pancreas from a case of bronzed diabetes. The parenchyma is divided into small groups, some of which resemble both acini and islands. × 190

the anatomy of the pancreas and the vascular arrangement and structure of the islands of Langerhans are fully described. It is perhaps sufficient here to note that they were originally thought to be nervous elements. They have been considered by Hansemann[2] as mesodermal in origin, and a number of the earlier authors[3] described them as lymphocytes. It has been shown, however,

[1] Jour. of Exp. Med., 1906, viii, 193.
[2] Zeit. f. klin. Med., 1894, xxvi, 191; Verhandl. der deutschen path. Gesellsch., 1902, iv, 187.
[3] Dieckhoff, Krause, Kuhn and Lea, Mouret, Pischinger, Pugnat, Renault, Sokoloff.

that the islands are derived originally from pancreas tissue. Kuster[4] described them as arising from the ducts, and Pearce[5] from the acinous tubules. Laguesse[6] also concluded that they were derived from the acinous tissue, but that they were transitory and might later assume the appearance of acini. The islands seem to be more numerous in the embyro than in the adult; thus, they have been considered as embyronic remains.[7] They also have been described as exhausted acini[8] and as acini changed temporarily, but which were capable of reverting back.[9] Minkowski has expressed the opinion that the number of islands increases during the period of activity of the pancreas and diminishes during the period of rest, and that every lobule at some time must pass through a "Stadium der Langerhans'schen Inseln."

The general opinion, however, and that which is included in practically all the recent works on this subject,[10] is that the islands are absolutely independent structures and elaborate some internal secretion. It is a peculiarly attractive theory and one which is supported by the very definite outline of the islands, as well as their more or less constant shape and number.

It is generally admitted that there are extensive variations in size, shape, and number of the islands; the type of their component cells and their arrangement are also by no means regular in different cases and even in adjacent islands of the same pancreas.

The following pictures are included as illustrative of some of these variations in the human pancreas (Figs. 3 to 11).

These pictures not only seem to show great individual variations in the islands, but also are suggestive of their mode of formation. Figs. 3, 4, 6, 7, and 10, appear to indicate that the islands are not always absolutely independent structures. Indeed, in almost every human pancreas, and even more commonly in the pancreas of rabbits, very intimate connections can be observed between the island trabeculæ and adjacent acini. By serial sections such connections may be demonstrated in some situation in practically every island. This may of course, be argued as a persistence of the original fetal connection.

In a large number of cases the capsule outlining the island is very indistinct, or absent, or may only be represented by a capillary. This capsule has been described as a special structure, but often groups of pancreas acini are surrounded in an exactly similar manner (Fig. 8). Indeed, the whole circulation in many

[4] Arch. f. mik. Anat., 1904, lxiv, 1.

[5] Amer. Jour. of Anat., 1903, ii, 445; Amer. Med., 1903, vi, 1020.

[6] Compt. rend. de la Soc. de Biol., 1894, xlvi, 667; Jour. de l'anat., 1894, xxx, 591; Compt. rend. de la Soc. de Biol., 1895, xlvii, 699; Jour. de l'anat., 1896, vol. xxxii, Compt. rend. de la Soc. de Biol., 1905, lviii, 504; Ibid., 1905, viii, 542.

[7] Gibbs, Harris, and Gow.

[8] Dogiel, Tschassownikow.

[9] Kollossow, Laguesse, Lewaschew, Minkowski, Saviotto, Statkewitsch.

[10] Diamare, Jarotsky, v. Ebner, Opie, Schultze, Sobolow, Sauerbeck, Lépine.

of these islands might be reconstructed from interacinous vessels which have become dilated in consequence of some atrophy of the

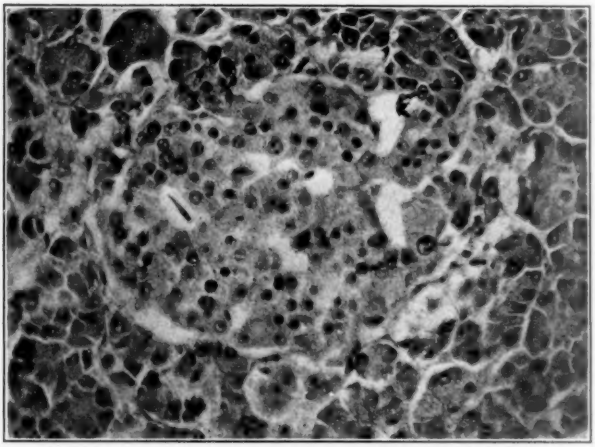

FIG. 3.—Island of Langerhans, composed of large cells arranged in trabeculæ, some of which are intimately related with the adjoining pancreas acini. (From a male, aged thirty-three years; died from pneumonia.) × 400.

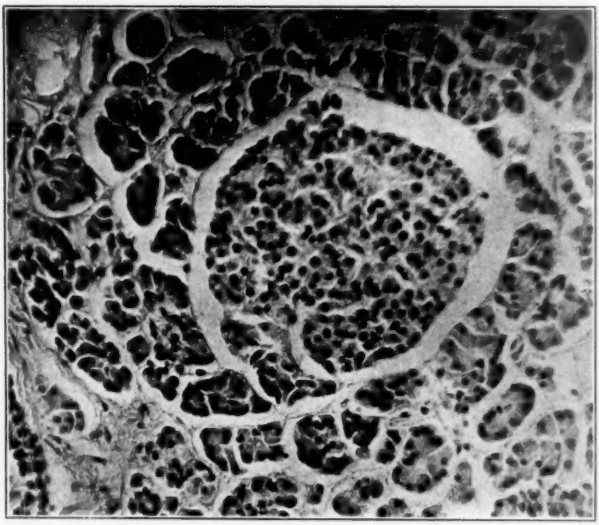

FIG. 4.—Island of Langerhans, composed of a solid mass of cells, which are, however, grouped in small masses. (From a female, aged thirty-seven years; died of mitral stenosis and thrombosis of the jugular and subclavian veins on the left side.) × 400

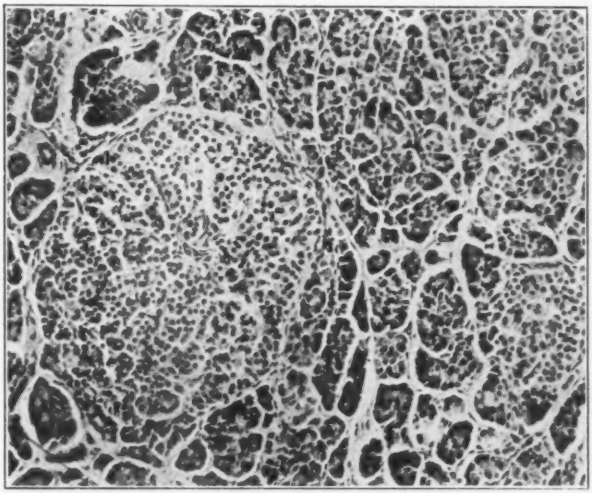

FIG. 5.—Large adenomatous island. Several of the pancreas acini show intimate relations with cell groups closely resembling islands. (Pancreas of a male, aged sixty-three years, weight, 121 pounds. Aorta slightly atheromatous. Died of acute general peritonitis following herniotomy operation.) × 230.

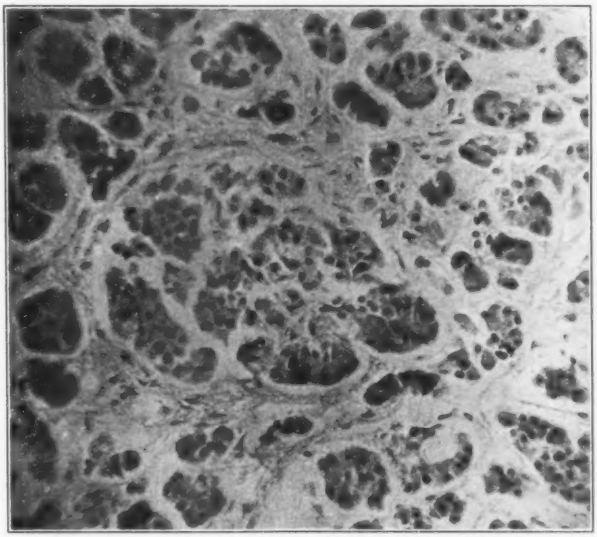

FIG. 6.—Island showing inclusion, within the capsule, of acinous-looking cells. (From a female, aged sixty-four years; died from a cardiac atrophy. No edema or cyanosis.) × 400.

acinous cells. In contradiction to what is usually noted, it might even be said that the circulation in the islands of Langerhans shows no essential difference from that in the rest of the pancreas.

The cells composing the islands commonly are arranged as a single layer along the vessels, but very frequently also the island has an acinous appearance (Figs. 4, 5, 9, and 10), and sometimes also the whole space is filled with cells with no particular arrangement (Fig. 4). In many cases portions of definitely acinous tissue are included among the island cells, an appearances which must not be confused with irregular islands extending among the acini (Figs. 6, 7, and 10). Apparently, also, there are very sugges-

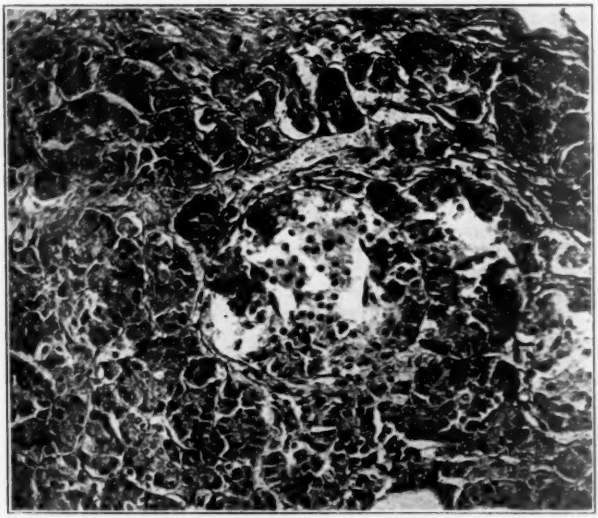

FIG. 7.—Island showing inclusion of definitely acinous cells intimately related to the island cells. (From a female, aged forty-nine years; died of mitral stenosis and gangrene of left leg from thrombosis.) × 280.

tive indications that in such cases the island cells are being formed by a catarrhal atrophic process from the acini (Fig. 6). Frequent pictures, however, are to be noted where the island cells are apparently becoming swollen and darker in their staining reactions and arranged more like ordinary acinous cells (Fig. 10). Mitoses have been described in the island cells, but in all our material none were found.

There are therefore, some indications, in contradiction to those who maintain the independent existence of the islands, that these structures have both intimate relationships with the pancreas acini and also that transitions in adult life are a distinct possibility.

Although these transition figures have been noted by a variety of writers, it has generally been considered that even if new islands are formed in the adult pancreas, they are developed for some function relating to carbohydrate metabolism.

This also has considerable interest in relation to the etiology of diabetes, as Opie,[11] Weichselbaum and Stangl,[12] Wright and Joslin,[13] Herzog,[14] Sobolow,[15] and many others accept the theory as justified

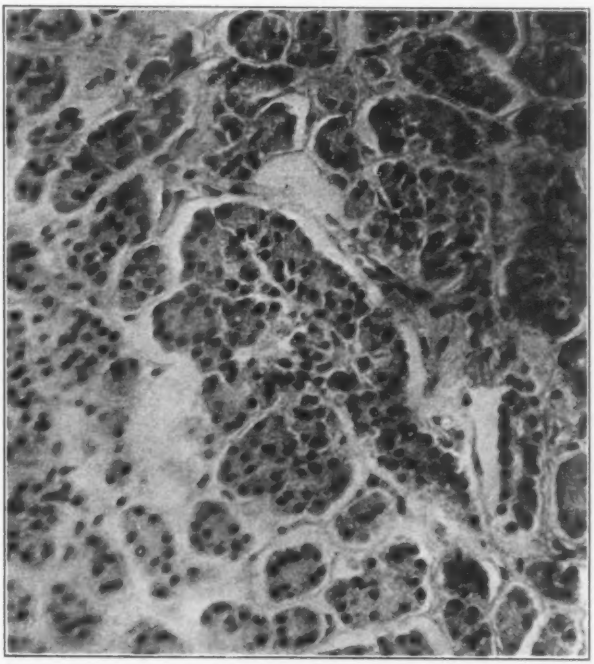

FIG. 8.—A group of pancreas acini isolated like islands. (From a male, aged fifty-nine years, weight, 119 pounds. Extensive arteriosclerosis. Died of a hypernephroma of the right kidney with metastases in the bones, brain, lungs, etc.) × 400.

that diabetes may be due to some change in the islands. Indeed, the relation of the islands of Langerhans to carbohydrate metabolism has largely been originated by the pathological reports of these investigators, particularly by Opie and those others who have described cases of diabetes with lesions in the islands alone. Cecil,[16] for instance, of 90 cases of diabetes, found 79 in which the

[11] Jour. Exper. Med., 1901, v, 397, 527.
[12] Wiener klin. Woch., 1901, xiv, 968.
[13] Jour. of Med. Research, 1901, vi, 360.
[14] Virchow's Archiv, 1902, clxviii, 83: Trans. of Chicago Path. Soc., 1901, v, 2.
[15] Ibid., 1902, clxviii, 91.
[16] Jour. Exp. Med., 1909, xi, 266.

islands were either hyaline or sclerotic, and in 12 of these the remaining pancreas was not especially affected. If it is admitted, however, that the islands of Langerhans are either undifferentiated or regressive pancreas acini, it is just such tissue which most likely would be affected by hyaline or sclerotic changes. The pancreas also is well known to be subject to extremely rapid postmortem change in consequence of which small patches of degeneration may be produced which very closely resemble the changes described in the pancreas of some diabetics. Indeed, the great bulk of pancreas autopsy material is useless for examination, and postmortem changes have to be very carefully considered in every case.

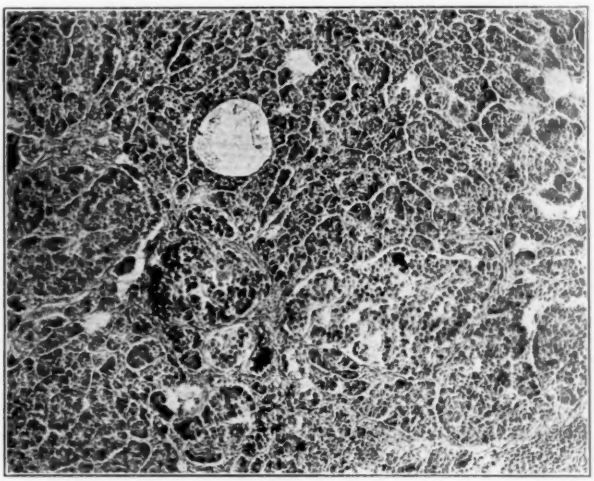

FIG. 9.—Pancreas showing a variety of types of islands. To the left an island is adenomatous in type; in the centre, an island contains almost typical acini. (From a male, aged sixty-six years; weight, 139 pounds; died from mitral stenosis, general venous stasis, and hydrothorax.) × 90.

A particularly strong argument for the island theory has been advocated from the results of ligature of the pancreatic duct. In such conditions, as is well known, there occurs extensive atrophy of the pancreas, and eventually, as is claimed by many observers, only islands of Langerhans persist. It has also been noted that ligature of the pancreatic duct is followed only very rarely by any glycosuria. Vassali (1891) was perhaps the first to perform this experiment. He noted a general glandular atrophy, but with preservation of the islands. In 1900 Schultze[17] confirmed this, ligating off small portions of the pancreas in guinea-pigs. After eighty

[17] Arch. f. mik. Anat., 1900, lvi, 491.

days he found only a few dilated ducts and normal islands. Since no glycosuria was produced his natural conclusion was strongly in support of the independent existence and internal secretion of the islands. Zunz,[18] in 1905, produced apparently the same condition in the pancreas of dogs. In 1901 Minkowski,[19] from similar experiments, concluded that the pancreatic tubules and islands both become atrophied as a result of the operation, and

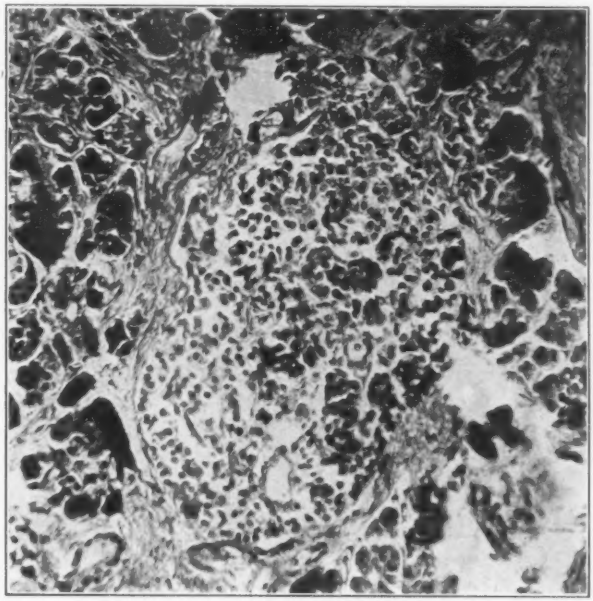

FIG. 10.—Large island of Langerhans, showing within it enlargement of some of the cells with acinous arrangement of these, like the formation of new pancreas acini. (From a male, aged forty-eight years; died of tabes dorsalis.) × 280.

Hansemann[20] (1902) had the same results. Excretory channels of the pancreas apparently tend to be readily reformed, and, as Dewitt[21] notes, this may account for the contradictory results obtained after ligature of the duct. The operation in many cases, as noted by Hansemann (1902) and Lombroso (1905),[22] does not by any means cause atrophy of the entire pancreas, so an absence of glycosuria is not conclusive evidence of the island theory.

[18] Zeit. f. allg. Path. u. path. Anat., 1905, xvi, 5.
[19] Arch. f. mik. Anat., 1901, lix, 286.
[20] Loc. cit.
[21] Loc. cit.
[22] Arch. ital. de biol., 1904, vol. xlii; Jour. de Phys. et de Path. gén., 1905, vii, 3.

Our own experience of the effects of ligature of the pancreatic ducts in animals is limited to 5 cats, 2 rabbits, 2 guinea-pigs, and 1 dog. In these animals the pancreas was ligatured at the point where it is reflected from the duodenum. So far as possible care was taken to avoid the bloodvessels, so that the result might not be modified in this way. In all of these much the same changes were produced. Even after forty-eight hours in a guinea-pig definite atrophic changes were found in the acini. After four days the atrophy of the acini was marked, but many of the islands could

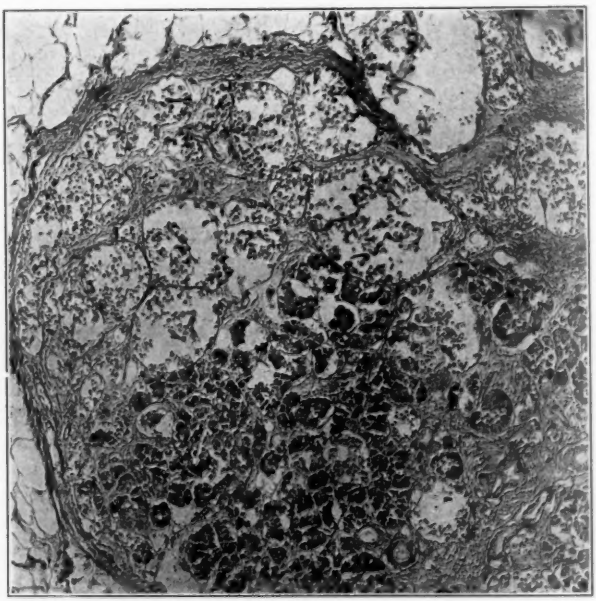

FIG. 11.—Section of a pancreas which seems to be almost entirely composed of islands. (From a female, aged forty-nine years, 105 pounds in weight. No arteriosclerosis. Died of mitral stenosis and gangrene of the left leg, probably from thrombosis.) × 80.

still be seen persisting in the atrophic lobules. In three weeks the acinous tissue had become very attenuated. It was isolated in small masses surrounded by fibrous tissue and no islands were distinguishable (Fig. 12). Both the islands and acini seemed to undergo a similar atrophy. No glycosuria was found in any case. There were, however, in some of the cases, particularly in the dog which was killed 9 weeks after the operation, occasional patches of healthy looking pancreas tissue which seemed to have escaped the atrophic process and which may have been responsible for the non-development of glycosuria. The persistence of comparatively small

portions of pancreas tissue is sufficient to prevent glycosuria. In dogs no diabetes results if only a narrow strip of pancreas tissue is left along the duodenum. In the cats, at any rate, there seemed to be no special preservation of the islands, and all that appeared to remain in the older standing cases were sub-groups of atrophied acinous cells.

It is also a difficult fact to explain why in a considerable proportion of diabetics, the islands are considerably reduced in number or may even be absent altogether. In one of our cases of a rapidly fatal diabetes in a man, aged thirty-five years, after a search through the greater part of the pancreas no islands were found. The pancreas acini in this case were extremely atrophic. This is at first

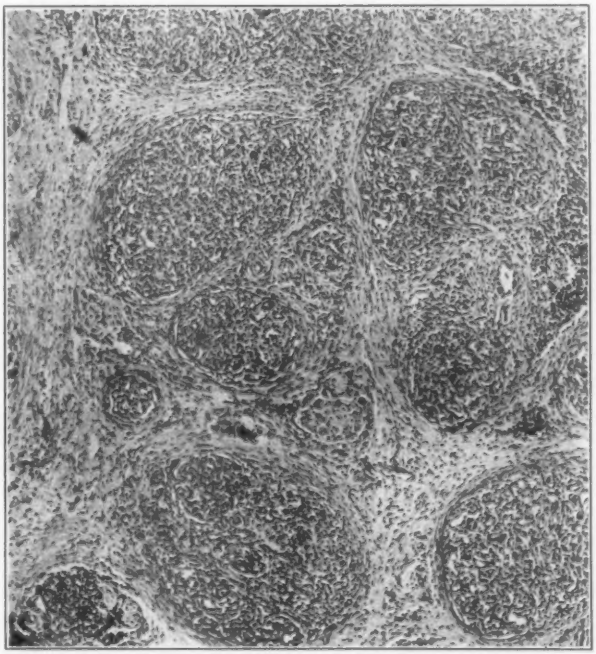

FIG. 12.—Pancreas of a cat whose pancreatic duct had been ligatured three weeks previously. The acini have become collapsed and atrophic. There has been an extensive development of fibrous tissue. No islands of Langerhans can be found among the atrophic acinous tissue. × 90.

strongly in support of the island theory, yet if these islands had been leading an independent existence some scars or necrotic remnants ought to remain indicating the positions where the islands were destroyed. These, however, were not noticeable.

It has thus also to be considered as possible that the islands are a reserve source for the formation of new pancreas tissue, and also that pancreas acini may revert in type to structures resembling or identical with Langerhans' islands. There are, then, a number of facts which are difficult to reconcile with the island theory and such observers as Hansemann,[23] Gutmann,[24] Reitmann,[25] Karakaschew,[26] Herxheimer,[27] Dieckhoff, Benda, and others have unhesitatingly condemned it. It is certainly difficult to credit the islands, whose total amount is so relatively small, and whose component cells at least appear to be so poorly specialized, with one of the largest functions in the metabolism of the body.

However one regards the etiology of diabetes, involvement of the pancreas has become the most important factor. It is diseased in the great majority of cases. In Cecil's[28] series of 90 cases it was described as unaffected in only 6. There is, however, no constant lesion in the pancreas which is associated with diabetes, as the pathological changes vary from general atrophy which in some cases is the result of arteriosclerosis, to necrosis and fibrous replacement of the organ. Hansemann[29] also has described 12 cases of diabetes due to occlusion of the pancreatic duct by stones. Similarly, gallstones impacted in the ampulla may also induce diabetes on account of marked inflammatory change in the pancreas, probably resulting from regurgitation of the bile salts into the pancreatic ducts.

It seems possible, therefore, that the pancreas is not merely an organ secreting digestive enzymes, but, in its entirety, has also important relations in carbohydrate metabolism. The pancreas does not seem to have any special relation to the formation of glycogen, as it has been shown that glycogen is formed in diabetes. Nischi's[30] work is confirmatory of this, as he injected glucose solution into one-half of the liver of depancreatized tortoises and found that the glycogen content of the injected half was greatly increased. It may be, of course, that the pancreas involves some internal secretion which regulates sugar destruction, yet, even more likely, it eliminates or destroys substances which when accumulated in sufficient degree by retention in the system, on account of deficient pancreas activity, are capable of producing abnormal disintegration of glycogen, etc., in the tissues and consequent diabetes. In support of this it has been shown by the researches of Arnheim and Rosenbaum, and by Feinschmidt, after removal of the pancreas in dogs, and apparently also in human diabetes, that the serum and tissues

[23] Loc. cit.
[24] Virchow's Archiv, 1904. clxxvii, Suppl., Heft 128.
[25] Zeit. f. Heilkunde, 1905, xxvi. 1.
[26] Deutsches Arch. f. klin. Med., 1904, lxxxii, 60.
[27] Verhandl. der deutschen path. Gesellsch. Erganzungscheft; Cent. f. path. Anat., 1904, xv, 215.
[28] Loc. cit.
[29] Loc. cit.
[30] Arch. f. Exp. Path. u. Therap., 1909-10, lxii, 173.

contain abnormal amounts of a glycolytic substance. Lépine (1905)[31] also observed after ligature of the pancreatic duct or injection of oil into it that the glycolytic power of the blood is greatly increased.

The serum of depancreatized dogs does seem to possess a considerably increased ability to convert glycogen into dextrose, as compared with normal serum.

Evidence is not yet complete enough to conclude that pancreas insufficiency is the primary factor in every case of diabetes, yet even at the present time it has assumed by far the most important place.

The relation of the liver to diabetes, if any, is difficult to understand. The symptom complex *Bronzed Diabetes* has been adduced by many writers to support the theoretical existence of a so-called "liver diabetes;" but a careful study of the reported cases hardly warrants such an assumption. Certainly lesions of every conceivable type and severity can affect the liver without the production of any glycosuria. In Simmond's[32] series of 144 cases of diabetes only 7 had liver cirrhosis. Those cases in which liver cirrhosis has been associated with glycosuria are, as Steinhaus, Lando, and others have shown, also cases in which the pancreas has been extensively diseased.

The possibility of cerebral diabetes is difficult to dispute. Undoubtedly lesions of the medulla are associated with glycosuria; but only very few diabetics show any demonstrable lesions in the brain. Vasomotor changes in the pancreas, as influenced through the centre in the medulla, may be the essential factor. Such conditions as fright may markedly increase the sugar output in a diabetic (an evident feature in our case); and adrenalin injections in animals may produce glycosuria. Both of these factors profoundly alter the vasomotor system and may act on the pancreas in this way.

It, of course, cannot be denied that they might not act similarly on the so-called sugar controlling centre of the brain, although Herter's observation that painting adrenalin on the pancreas was associated with glycosuria much more rapidly and extensively than by any other mode of administration, is somewhat contradictory.

To Hanot and Chauffard, in 1882, belongs the credit of having first noted the disease condition known as bronzed diabetes, although some years previously Trousseau[33] had reported the autopsy on a diabetic with a bronzing of the face and nearly black discoloration of the penis, and found a greatly enlarged cirrhotic liver of a grayish-yellow color; and Troisier, in 1871, described a case under the title of "diabéte sucré."

[31] Compt. rend. de la Soc. de Biol., 1903, lv, 161; Jour. de Phys. et de Path. gén., 1905, vii, 1.
[32] Berl. klin. Woch., 1909, xli, 531.
[33] Clinique méd., 2d edition, ii, 627.

The symptom complex which they described had a triad of symptoms—pigmentation of the skin, cirrhosis of the liver, and diabetes. These, however, do not occur simultaneously and cases are described varying in every way as to the primary event. The present-day opinion seems still to agree with that of Hanot, Marie, and others of the earlier authors that bronzed diabetes is not a mere modification of diabetes, but a true pathological entity.

The bronzing is perhaps the most conspicious sign. It is due to the deposit of pigment, mostly hemosiderin, but partly non-iron containing, in the tissues. This variety of pigmentation was originally termed hemochromatosis by v. Recklinghausen in 1889. It is a blood derivative, yet the degree of anemia, if any, is, as a rule, very slight. On account of this relatively slight anemia it has been considered that there is, as Meltzer has advocated, a defective elimination of normally destroyed blood. There certainly must be defective elimination of some sort, because the liver in practically every case of hemochromatosis has been described as diseased in one way or other. A number of cases (8, 7, 14, 17, 28, 32, 39, 40, in list) have been described, it is true, by various observers where there have been hemorrhages in some situation or other during the disease. This, however, is not the rule, and is no more than can be observed in any series of liver cirrhosis cases. Unfortunately we did not procure a specimen of the bone marrow from our case, but in the sections of the various organs there was no evidence of blood regeneration. The sections of bone marrow in one of Sprunt's cases showed "practically a normal picture;" in the other the marrow was "slightly hyperplastic, but there was nothing to indicate any unusually active hematopoiesis."

Probably, however, there is also some excessive blood destruction, as the accumulation of pigment is often enormous, and in some cases it has been very extensive within a short period. Generally the destruction of blood must be slowly accomplished to permit of the more or less complete regeneration and the high blood counts usually recorded.

The general opinion (Jeanselme, Berg, Buss, Anschutz, Doutournier, Marie, etc.) seems to be, as expressed by Futcher, "that the pigmentation of the viscera is primary and antidates the diabetes," and "that the deposition of the hemosiderin in the cells of the liver and pancreas and of the hemofuscin in the connective tissues of these glands eventually leads to the large, cirrhotic, pigmented liver and the sclerotic pancreas, which are so characteristic of the disease."

This idea of hemochromatosis being the primary event is neither easy to understand nor to prove. It presupposes blood destruction from some unknown cause. Clinically, in Futcher's second case, as in several others, the first sign was pigmentation, but considering the well-known latency of symptoms of many diseases, notably

cirrhosis of the liver, it is impossible to be certain that the blood destruction and pigmentation are the primary events.

There is undoubtedly a deposit of iron containing pigment in the tissues in many other diseases, as pernicious anemia. Hintze[34] has described 5 cases of extensive hemosiderin pigmentation of the viscera in tuberculosis and carcinoma, and Goebel[35] has noted a similar condition in a case of carcinoma of the stomach. Tillmanns[36] described a case of a man, aged seventy-six years, who died two months after having sustained a fracture of the pelvis and a ruptured liver, and at whose autopsy a general hemochromatosis of the viscera was found. Osler also has noted pigmentation of the skin in 6 out of 15 cases of splenic anemia. In exopthalmic goitre also, there frequently is found some excess of cutaneous pigmentation, and its distribution is about the same as in bronzed diabetes cases.

In cases of bronzed diabetes the only constant, co-existing, anatomical lesions seem to be hepatic cirrhosis and sclerosis of the pancreas. In some of the recorded cases the liver has simply been noted as enlarged. Most of these probably were cirrhotic, although it must be remembered that in many diabetics the liver is enlarged from fatty change. Glénard noted that the liver was enlarged in 32 per cent. of all diabetics. These two organs have been thus blamed for the production of the hemochromatosis. Brault and Gaillard have considered the liver cirrhosis as primary and the blood degeneration as a result, and Kretz stated that the liver disease and blood destruction were coördinate events. Hess and Zurhelle also have noted the liver cirrhosis as primary, then the hemochromatosis, and finally diabetes. Rössle[37] believed that the blood destruction was due to a capillaritis and an abnormal phagocytic activity of the liver cells, and the pigment thus produced by the blood destruction in the liver was disseminated to the other organs. Rössle's work is, however, by no means convincing. Undoubtedly, blood cells are commonly found in various pathological conditions in the liver cells, but mostly in a degenerate state. It is also difficult to imagine any spontaneous sudden phagocytic activity of the liver cells for red cells alone, and if it did occur, why hemochromatosis should be so rare.

Osler, Opie, and others have advocated that the pigment is formed in the liver and disseminated from it to the other organs. Létulle, although holding that diabetes was the primary factor, claimed that the pigment was formed where it was found deposited.

Beattie also, although not claiming any phagocytic activity for

[34] Virchow's Archiv, 1880, lxxix, 492.
[35] Ibid., 1894, cxxxvi, 482.
[36] Arch. d. Heilkunde, 1878, xix, 119.
[37] Ziegler's Beiträge, 1907, xli, 181.

the liver, stated that the pigment is elaborated in the liver and pancreas and disseminated from there, and by its irritation was responsible for at least some of the fibrosis in these organs.

Diabetes has been considered by many, particularly Hanot and Schachmann, Hernandez, Mossé, Massary, and Potier, to be the primary condition and the source of the blood destruction and hemochromatosis. Diabetes, however, only very rarely is associated with hemochromatosis. Futcher notes that of 256 cases of diabetes, only 2 were bronzed. Also a number of authors—including Létulle, 2 cases; Brault, 2; Osler,[38] 2; Opie,[39] 1; Abbott,[40] 1, and Hintze, 3 cases—have described hemochromatosis and liver cirrhosis unaccompanied by diabetes.

The suprarenals have been claimed to have important relationships to the production of hemochromatosis. Blum,[41] as the result of his being able to produce glycosuria by adrenalin injections, came to the conclusion that lesions of the suprarenal played an important role in the production of bronzing of the skin in some cases of diabetes. The suprarenals were noted as abnormal in the cases of Mossé and Daunic, and of Rabé, and it has been contended that hemochromatosis is due to some defective control of pigmentation by the suprarenals. With the exception of Rabé's case, where the adrenals were tuberculous, the changes in the suprarenals described in the above cases were only what might be found in any autopsy. Neither the cutaneous nor visceral pigmentation of hemochromatosis appears to be in any way allied to that of Addison's disease.

The clinical record of the present case is of some value in the time relation of the pigmentation, as it did not appear until some years after evidences of liver cirrhosis and symptoms of diabetes had appeared. It must, however, be remembered that the skin in hemochromatosis is probably the last site to be pigmented. In the cases of Wille, Kretz, and Létulle there was extensive pigmentation of the internal organs, but none was noted in the skin. In many cases the pigmentation evidently either escapes observation or is regarded as merely the result of exposure to the sun's rays, and so fails to attract especial attention. In our case it had not been noted by other physicians previous to our first examination, and the patient's wife had supposed his color was nothing but sunburn. Neither the family physician nor the family had noted any pigmentation in Blumer's case. The pigmentation of the skin is always much less than that of the other organs.[42] It may

[38] Brit. Med. Jour., 1899, ii, 1895.
[39] Diseases of the Pancreas, 1910, p. 368.
[40] Trans. Path. Soc., London, 1900, li, 66.
[41] Deut. Arch. f. klin. Med., 1901, lxxi, 146.
[42] In Abbott's case (without diabetes and the only unquestioned case of hemochromatosis in a woman) the skin pigmentation was very slight.

be that before the skin pigmentation becomes obvious clinically, exposure to sunlight and the production of some dermatitis is necessary. It is certain that in most bronzed diabetes cases, the pigmentation is chiefly on the exposed part of the body.[43] Possibly this accounts for the fact that almost every case of hemochromatosis with skin bronzing has been described in males. The greater opportunity for exposure and the natural dryness, as well as the greater tendency for dermatitis, may account for the bronzing in general hemochromatosis to be almost exclusively in males. In addition, the type of cirrhosis commonly described in hemochromatosis is also relatively more frequent in males. Besides Abbott's case, in a woman without diabetes, Berg[44] and Murri have also published female cases, but of these, Berg's case later came to autopsy, and there was no mention of hemochromatosis, and Murri's case exhibited pediculi and was discharged with normal skin and normal urine.

The pathological records of our case argue against the theory that the pigment accumulation is the cause of the inflammatory process in the various organs because the pigment evidently was largely deposited in the spared parenchyma cells of the liver and pancreas, and to a relatively much less extent in the connective tissues of these organs. The kidneys, thyroid, heart, etc., were all extensively pigmented, yet were hardly at all involved in any cicatricial process. It is doubtful, indeed, if blood pigment has any marked tendency to cause inflammatory processes. Hematoidin certainly seems to exist in large amount in the liver cells and in the heart muscle without producing any extensive damage in these organs.

In almost every case of liver cirrhosis there is some iron-containing pigment in the liver cells, and often a small amount in the other organs also. This is only natural when one considers that liver cirrhosis is caused by some toxic process which at the same time might readily cause blood destruction. Also, the accumulation of substances not eliminated by the liver may be a source of considerable hemolysis. The rarity of general hemochromatosis in sufficient degree to cause skin bronzing can only be explained by assuming that only rarely is there sufficiently extensive blood destruction in liver cirrhosis.

The relationship of diabetes to liver cirrhosis seems more easily established. In from 2 to 4 per cent. of all cases of liver cirrhosis

[43] Whether the pigmentation ever diminished in intensity upon lack of exposure to the sun cannot be stated. In our case the bronzing lessened, but the grayish-blue color increased as time went on and the patient was more confined to his room and bed. In a second case which we have studied, and which has not yet been proved by autopsy to be a case of hemochromatosis, there has been a very marked change, since his weakened condition and later occupation have kept him most of the time within doors; in fact, the pigmentation has practically disappeared. In Murri's the pigmentation cleared up during patient's two years residence in hospital.

[44] Med. Rec., 1899, lvi, 881.

there is diabetes, and of all diabetics about 5 per cent. are associated with signs of liver cirrhosis. In such combinations there is not necessarily any hemochromatosis. Barth,[45] for instance, has described such a case without any pigmentation. As Steinhaus,[46] Lando,[47] and others have shown, and in our own experience, the pancreas is commonly involved in liver cirrhosis cases. The pancreas may become damaged by the same process which causes the liver cirrhosis, or it may also be that the catarrhal processes so common in the bile ducts in liver cirrhosis may involve the excretory channels of the pancreas and induce secondary atrophic and sclerotic changes in that organ. Sprunt considers hemochromatosis to be "a metabolic disease implicating many of the body tissues and manifested, especially, by a change in the chromogenic groups of the proteid molecule with the deposition of pigments." He refers the diabetes to the diminished oxidative power of the body due to pronounced disturbances in the iron containing constituents of the tissues, assuming these iron compounds to be catalytic agents in oxidizing processes." Much further clinical and experimental investigation must be carried out before the chromogenic groups of the protein molecule are held accountable for this condition, and still more to interpret the cause of the change. As far as the etiology of hemochromatosis has been studied nothing very helpful is to be learned from the previously recorded cases. Infections which might be responsible for the blood destruction, such as tuberculosis, sepsis, parotitis, and pyorrhea are very frequent in the described cases, but hardly commoner than terminal conditions in diabetes and cirrhosis of the liver. Malaria also is noted in a number of the cases, yet could not be considered an important etiological factor. Excess of alcohol is mentioned as a possible cause in a large proportion of cases, but in several it had no connection whatever.

From what may be gathered in the literature and from the study of our own case, it would seem as if today we are warranted in stating only that cirrhosis of the liver is the primary condition; that pancreatic involvement with diabetes is a sequence or coincident event to this; that the hemochromatosis, always in slight degree in liver cirrhosis, is in some cases very excessive and causes a general pigmentation which eventually also involves the skin; and finally, that the whole process is not any definite symptom complex, but a chain of circumstance which rarely seems to be completed.

[45] Bull. Soc. Anat., 1888.
[46] Deut. Arch. f. klin. Med., 1902, lxxiv, 557.
[47] Zeitschr. f. Heilkunde (Path. Anat.), 1906, vol vii

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6. De Massary and Potier, Soc. Anatomique, April, 1895	1
7. Jeanselme, Soc. Méd. des hôpitaux, 5 Fer, 1897, La Presse Médicale, 1897, No. 11	2
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13. Kretzl, Beiträge zur klin. Med. Chirurgie, Wien, 1896, Heft 15	2
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33. Wyss, Korr. f. Schweize Arste, 1899, xxix, 559	1
34. Martineck, Charité Annalen, 1909, xxxiii, 40	1
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36. Lando, Zeit. f. Heilkunde, 1906, Neue Folge 1, p. 7, Case 6	1
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38. Futcher, Amer. Jour. Med. Sci., 1907, cxxxiii, 78	2
39. Blumer, Trans. Conn. Med. Soc., 1911	1
40. Sprunt, Archiv. Int. Med., 1911, vol. viii, p. 75.	2
	51

Doubtful.

Heller, Deut. med. Woch., 1907, p. 1216	1
Murri, Wien. klin. Rundsch., 1901, ii, 345	1
Palma, Berl. klin. Woch., 1893, p. 815	1
	3

A second case of writers', male, aged forty-nine years, pigmented four years, skin section contained pigment giving iron reaction. Diabetes, two years. Liver much enlarged and nodular. Ascites, two years.

REPORT OF A CASE OF LOUD VENOUS HUM HEARD OVER THE XIPHOID CARTILAGE IN CIRRHOSIS OF THE LIVER. AUTOPSY.[1]

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Murmurs heard in the epigastrium in cirrhosis of the liver have been observed by many clinicians. Most of these have been of venous origin, and, being more or less confined to the region of the umbilicus, have been thought to be due to enlarged umbilical or para-umbilical veins. In some instances such conditions have been proved by autopsy.

The case of which the following is a history is of great rarity, and I have found but two similar ones on record, though in neither of these was an autopsy obtained, so that the anatomical similarity must remain conjectural. W. S. Thayer[2] reported a case under the following heading: "Report of a Case of Venous Hum heard in the Epigastrium in a Case of Cirrhosis of the Liver," and his study of the literature, from which I quote, yielded but one other case in which the murmur was similarly situated, and in which the same theory might account for the phenomenon.

The case here reported came under my observation in the wards of the Philadelphia Hospital on the service of Dr. F. P. Henry.

The history of the patient is as follows:

W. T. J., aged seventy years, male, stone cutter, machinist, and watchman.

Family history of no significance.

Social History. The man gives a history of excessive use of alcohol for a long period of years. Takes whiskey and beer frequently, and has been accustomed to the taking of whiskey on an empty stomach in the early morning.

Previous Medical History. Thirty-five years ago he had a severe attack of articular rheumatism, confining him to bed for some six weeks. Since that time he has had numerous more or less similar attacks. Four years ago the patient was confined to his bed suffering from dyspnea and edema of the extremities.

Present Illness. His present illness dates from a period about four months ago, when he noticed that he tired easily and became short of breath on exertion. Three months ago he was compelled to give up work of any kind. The dyspnea has gradually grown

[1] Read before the Medical Section, College of Physicians, Philadelphia, May 11, 1911.

[2] Amer. Jour. Med. Sci., March, 1911.

worse, and he is now unable to go about. Two months ago he noticed his abdomen was swollen.

Physical Examination. Chest is emphysematous in appearance. The abdomen is full, and two veins stand out conspicuously, running more or less parallel from the middle of each groin, and anastomosing at a point between the umbilicus and ensiform, and a little to the left of the median line. Here there is a large varicosity from which a number of veins spring and travel upward over the ribs and sternum, and may be seen as high as the second rib. These veins empty with inspiration, and seem also to have another rhythm, possibly in some relation to the cardiac cycle. Pulses are equal.

Percussion over the lungs is normal except for a wooden note. Auscultation is negative.

The heart shows a little hypertrophy, and a systolic murmur is heard at the apex as well as at the aortic cartilage, the latter being transmitted into the carotid arteries. Over the ensiform cartilage is heard a very loud roaring murmur, which is localized to an area scarcely exceeding the space covered by the head of the stethoscope. This murmur is continuous, but has remissions in its loudness, there being a distinct inspiratory accentuation and a corresponding expiratory lessening. The murmur can be readily made to disappear by light pressure of the stethoscope. The liver dulness is apparently about normal, although a slight quantity of fluid and gaseous distention of the abdomen interferes with accurate determination of the lower border of liver dulness. There is some edema of the ankles.

The subsequent history in brief was that on May 7, 1911, the man rather suddenly became delirious and very ill, and on May 12, 1911, died of pulmonary edema. There was no increase of the ascites, which at no time reached large proportions, a fact possibly due to the free venous anastomosis. The roaring murmur, however, disappeared altogether for a time, but was faintly heard afterward.

Autopsy. At my request the prominent superficial veins were injected with a starch solution colored with methylene blue. An unsuccessful attempt was also made to inject the internal mammary vein.

The following notes are taken from the autopsy record in part, and the more minute description of the sinus was given me by Dr. McConnell, who made the autopsy.

Just beneath the ensiform cartilage are dense adhesions to the anterior margin of the liver. Within this mass of adhesions is a large venous sinus, the branches of which pass down into the adhesions. The spleen is bound down by adhesions. Elsewhere the peritoneum is smooth and transparent.

Heart. Aortic leaflets rigid and contain deposits of lime which extend well up from the bases of the leaflets.

Liver. This organ is small and pale, with a markedly roughened surface. It is firm and cuts with difficulty, leaving a granular surface. On section the surface is gray, with small brown areas scattered throughout.

Gall-bladder. This is greatly distended; full of thick, brown fluid. The cystic duct is obstructed.

Underlying the ensiform cartilage and extending to the articulation with the sternum there is found a venous sinus about 7 mm. in diameter. Anteriorly there could be seen through an opening in the ensiform the anterior wall of this sinus. Proceeding from this opening were several small, superficial veins, probably in communication with the sinus. From this sinus there was a vein communicating with the vein in the suspensory ligament of the liver; this latter was somewhat dilated. Apparently there was no communication between the portal vein or inferior vena cava.

The entire lesion was contained within the mass of adhesions, between the anterior portion of the liver near its edge and the overlying ensiform and lower part of the sternum. The area occupied by the mass was about 4 by 2½ c.m.

These continuous loud murmurs are usually of venous origin, and are supposed to originate from small veins flowing into larger ones. The sound in this case must have been transmitted from the sinus to the surface by the small veins which perforated the ensiform and approached the surface.

The extreme localization of such a surprisingly loud sound was interesting and difficult to explain, unless due to the fact that the sinus was not in direct contact with conducting surfaces, being buried in a mesh of adhesions. For the same reason, perhaps, no thrill was present. It was impossible to identify this mass with any known vessels. It was apparently not connected with the vein of the round ligament, which in turn was enlarged.

The author suggested the possibility of the sinus being an anomalous ductus venosus, but such a theory could not be proved, as careful dissection was impossible.

Charcot is authority for a statement that venous hums in cirrhosis of the liver are of favorable portent, and one might be tempted to go farther and form a corollary to this proposition by stating that the disappearance of such murmurs is of evil omen. In our case, and also in Thayer's, the disappearance of the murmur meant the beginning of dissolution.

TUBERCULOSIS AMONG PHYSICIANS.

WITH REPORT OF ONE HUNDRED CASES.

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I have been under the impression for a long time that physicians fare rather better than the average patients among the laity when attacked with pulmonary tuberculosis. This study of the disease in 100 physicians who have been under my care during the last fifteen years is intended to test the correctness or falsity of this impression. Theoretically, the prognosis among medical men should be better than in others because of their familiarity with the earlier indications of the disease, and their knowledge of the supreme importance of early and correct treatment. For the same reasons those failing to obtain complete restoration to health should yet live longer than average lay patients.

In this tabulation no cases have been included in which the disease was so recent in origin as to make its classification as to possible recovery open to serious doubt. The 100 cases have naturally been from various parts of the world, and presented themselves in all stages of the disease. Five of them were females.

At the time of my first examination they were classified as follows: Incipient, 46; moderately advanced, 20; far advanced, 34. Of the incipient cases, there were 28 instances of complete arrest of the disease—a percentage of 60 plus among this class. Of the second stage, 3 underwent complete arrest, a percentage of 15. No recoveries were noted in the third stage cases. The recovery rate for the entire number thus stands at 31 per cent.

Many of the cases in the second and third classes had been ill for several years before coming to Colorado. The high recovery rate in the first stage cases gives ground for the assumption that the patients first seen in the second and third stages would have vastly improved their chances by earlier climatic treatment.

The death rate stands as follows: First stage, 5; second stage, 12; third stage, 22; a percentage of 39. It must be understood that these are not at all the final figures in the series, since the results are unknown in 10 cases, which have drifted away, and in 4 others who were improving when last heard from. Further, 9 physicians are living and practising, although still presenting abundant evidence of active tuberculosis, and 7 are living, but too ill to practise. Those in the last two classes, 16 in number, are beyond the possibility, practically speaking, of recovery, and probably the unknown 10 all belong in this category. Thus, we shall not err very seriously if we state the eventual mortality as

39 (dead) plus 10 (unknown) plus 9 (living and practising, all still under observation, and all, in my opinion, hopeless so far as recovery goes) plus 7 (too ill to practise), a total of 65. The 4 improving at last accounts we shall not attempt to place.

A more cheerful light is thrown upon the statistics given, by the statement that among the 9 still living and actively practising, but with active disease, the duration has averaged about thirteen and one-half years, the extremes being five years and nineteen years. Of the 7 still living but too ill to practise, the average duration of the disease is twelve years, the extremes being three years and twenty-one years. Of the 33 cases already dead, the duration of whose disease is known, the average time was five and seven-tenth years. The extremes were less than a year in 2 cases, and twenty-five years in one case. It would appear that far less than an average proportion of cases of acute pulmonary phthisis with quickly fatal outcome has presented in this series, probably because such cases are less apt to seek climatic treatment than the more chronic forms. It is to be noted that the third stage cases, still living after many years, or who practised for many years, have been generally of the fibroid type.

The results, classified according to the age of infection, are shown in the columns below:

	18 to 25 yrs.	26 to 30 yrs.	31 to 35 yrs.	Over 36 yrs.	Total.
Recovered	10 (26.3%)	12 (38.7%)	5 (35.6%)	4 (23.5%)	31
Died	18 (47.3%)	8 (25.8%)	6 (43.0%)	7 (41.0%)	39
Living and practising	4	4	..	1	9
Living not practising	1	3	1	2	7
Improved when last heard from	1	2	1	0	4
Unknown	4	2	1	3	10
	38	31	14	17	100

In only 3 of the cases noted as recovering has the duration of complete arrest been less than five years, and in these 3 it is three years or over. The best prognosis is evidently found in those contracting the disease between the ages of twenty-six and thirty-five years, and the worst in those under twenty-five years.

Several instances of rapid failure and death following marriage before complete arrest of the disease were noted in the series.

I have mentioned elsewhere the danger from tuberculosis to the physicians in the natural gas regions. It is occasionally contracted or becomes suddenly active after prolonged attendance, as at confinements, in houses heated by this means far above the proper temperature, and generally but poorly ventilated. Two physicians in this series dated the origin of their trouble from the severe cold taken while driving home in a winter night after such an experience.

One physician had 200 hemorrhages in eleven years, and finally succumbed. In the early part of his disease he once drank three hundred dollars worth of whisky in seven months. Another had

more than 60 hemorrhages. One died of hemorrhage after a twenty-five-year struggle with fibroid phthisis. Another died from sudden hemorrhage after material improvement from the draining of a large cavity at the base of the lung. In 2 instances the direct cause of death was tuberculous meningitis.

No recovery was noted among the several physicians who had contracted the disease in our tropical possessions, nor have I seen recovery in any other patient whose infection originated in these regions.

I had intended to compare the results among the physicians with those among 1000 laymen taken consecutively. Because of the fact, however, that a majority of the latter were seen for purposes of diagnosis, or advice as to climatic treatment, and thus were under care for but a brief period, the records were too incomplete for use in this way. The physicians, on the other hand, have commonly kept me posted as to their condition, a large proportion being engaged in active practice in the Rocky Mountain region at the present time.

I am satisfied in my own mind that the figures presented offer strong evidence that the recovery rate among physicians coming to Colorado is a high one; that the longevity after contracting the disease is above the average; and that still better results will be obtained when yet earlier diagnosis meets with more prompt and efficient response in treatment.

I am under obligation to my associate, Dr. T. R. Love, for the tabulation of the results presented in this article.

THE HIGH CALORY DIET IN TYPHOID FEVER: A STUDY OF ONE HUNDRED AND ELEVEN CASES.

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In 1909 Dr. P. A. Shaffer and the author[1] published the results of an investigation of the protein metabolism in typhoid fever. This investigation proved that by the use of diets of high caloric value, especially when rich in carbohydrate, it was possible to diminish, and, if the supply of carbohydrate was sufficient, to prevent the febrile loss of body protein, which on all previous diets had been so characteristic of this disease.

[1] Arch. Int. Med., 1909, iv

On the basis of this investigation a new diet was arranged for the treatment of typhoid fever. But no attempt was made in the paper referred to to discuss the therapeutic value of the diet.

A brief clinical paper[2] upon the subject was also published in 1909, but, in this paper, it was not possible to consider in sufficient detail either the diet or its administration.

In the four years which have elapsed since the investigation was begun, the high calory diet has been employed in the treatment of 111 cases of typhoid fever in the wards of the Second Medical Division of Bellevue Hospital. The experience derived from these cases forms the basis of the present paper. While it is my purpose to consider mainly the clinical application of the high calory diet, it will be necessary to refer from time to time to the scientific aspects of the subject.

THE DAILY FOOD REQUIREMENT. Shaffer and Coleman calculated theoretically the minimum daily food requirement of the average adult typhoid fever patient to be about 40 calories per kilogram of body weight, or approximately 3000 calories for a patient weighing 150 pounds, but their investigation showed that, in the cases studied, a mixed diet furnishing this amount of energy was not sufficient to establish nitrogen equilibrium. The best results in the maintenance of nitrogen equilibrium were obtained with diets furnishing from 60 to 80 calories per kilogram per day, or from 4000 to 5500 total calories. The optimum requirement, however, varied greatly in different cases and at different stages of the disease, but was always greater than the calculated minimum.

Grafe[3] found recently, in a study of the total metabolism of 12 cases of typhoid fever in the fasting state, that the heat production amounted only once to 40 calories per kilogram (the total in this instance being 1740), and never exceeded 2798 calories a day.

While the discrepancy in these results is accentuated by the fact that Grafe's patients were fasting, it cannot, with our present knowledge, be explained. But, on the basis of clinical experience and of our own laboratory results, I believe, and for the purposes of this discussion shall assume, that the more nearly nitrogen equilibrium is attained—in other words, the more perfectly nutrition is maintained—the greater are the chances in the patient's favor. Accordingly, I shall place the daily requirement of the average adult typhoid fever patient at more than 40 calories per kilogram, but would emphasize the statement that the optimum amount of food can be determined only by the needs of each patient individually.

Patients of small stature, including children, require more energy per kilogram, but not necessarily more actual energy, than average adults, because of the disproportion of surface area to weight.

[2] Coleman, Jour. Amer. Med. Assoc., 1909, liii, 1145.
[3] Deutsch. Arch. f. klin. Med., 1910, ci, 209.

THE PROTEIN, FAT, AND CARBOHYDRATE RATIOS. The next question requiring consideration is the relative proportions of protein, fat, and carbohydrate which should enter into the diet of the typhoid fever patient. So little is known concerning metabolism in typhoid fever that a full discussion of the ratios would of necessity be largely theoretical, and therefore unsuited to a paper of this character.[4]

Protein. The best results in the sparing of body protein obtained by Shaffer and Coleman were with diets containing from 10 to 15 grams of nitrogen, or 62 to 94 grams of protein, a day. Since Grafe essentially confirms these results, this quantity may be accepted provisionally as the optimum protein ration. But it is not improbable that the requirement varies in different stages of the disease, and that even in cases where nitrogen equilibrium has been maintained during the febrile period, there may be an increased demand for nitrogen during convalescence to repair the damage inflicted upon the tissues by the endotoxin.

Gelatin. Tissue protein cannot be built up from gelatin; therefore gelatin alone cannot supply the nitrogen needs of the body. But Murlin[5] has shown that two-thirds of the minimum daily protein ration may be replaced by gelatin, provided the carbohydrate supply is sufficient, without detriment to health.

While I have used gelatin only to a limited extent, there is no apparent reason why it may not be permitted as a part of the diet for the sake of variety.

Fat. We possess very little knowledge of the fat requirement in typhoid fever. But physiological economy would appear to make it expedient in fever, as in health, that a portion of the energy of the food should be supplied in the form of fat. Clinical evidence indicates that the fat needs of the typhoid fever patient vary in different stages of the disease. Many, if not the majority of patients, are able to take more fat in the steep-curve period and in convalescence than in the earlier stages of the disease. Fat has often furnished in these periods one-half of the total energy of the food of the cases in the present series, and the patients have appeared to be the better for it.

Carbohydrate. Of the three classes of foodstuffs, carbohydrate plays by far the most important part in preventing the consumption of the body tissues in fever. Grafe's studies on the total metabolism of fasting typhoid fever patients agree with the results of Shaffer and Coleman in establishing this fact. It has been found that the amount of carbohydrate necessary to protect the body protein varies in different subjects and at different stages of

[4] Certain phases of metabolism in this disease are now under investigation with the aid of the Benedict respiration apparatus.

[5] Amer. Jour. Phys., 1907, xix, 285.

the disease, therefore only a general recommendation can be made for clinical purposes; that the greater portion of the energy of the diet should be supplied in the form of carbohydrate, unless there is some definite indication to the contrary. A number of patients in this series have taken from 30 to 60 carbohydrate calories per kilogram per day.

PREVIOUS DIETS. While it will not be possible to discuss at length the different diets which have been employed in the treatment of typhoid fever, a brief summary of them may be given. Three types of diet have been used: (1) The meat-broth-carbohydrate-water diet of Graves, which furnished, at the most liberal estimate, not more than 300 calories a day; (2) the milk diet, from which the patient receives about 1300 calories a day, assuming that he takes two quarts; and (3)the so-called liberal diets. These diets furnish at most only about 2000 calories a day. They were constructed upon empirical data, and, as might be expected, are open to criticism. More attention has been devoted to increasing the variety of foods allowed than to the dynamic value of the diet as a a whole. Likewise, undue emphasis has been placed upon the necessity of increasing the protein.

The history of the typhoid diets thus indicates a definite though gradual tendency to raise the energy value of the food. The change from Graves' diet to milk added approximately 1000 calories a day to the patient's dietary; the change from milk to the liberal diets added about 700 more. But according to the results of Shaffer and Coleman, the most generous of these diets falls short of the patient's needs by about 1500 to 2000 calories a day.

THE SELECTION OF THE DIET. The most important considerations governing the selection of foods for the typhoid fever patient are their digestibility, absence of harmful residue, fuel value, and palatability.

Protein Foods. The choice of protein foods lies among the meats, eggs, milk, and the proteins contained in the carbohydrate foods.

Meats. The objections which may be brought against meat and preparations of meat raise the question whether they should be given at all to patients suffering from typhoid fever. Meats differ so much in digestibility, according to variety, "cut," method of cooking, etc., that it is difficult to make a comprehensive statement regarding them. Some meats are relatively indigestible in health; others appear to be digested readily even in disease. Probably the majority of physicians believe that patients suffering from febrile diseases are better off without meat. When meats are allowed to fever patients, there is likely to be an excess of protein in the diet, and Ewing and Wolf[6] have shown that a relative excess

[6] Arch. Int. Med., 1909, iv, 330.

of protein may cause serious disorders of metabolism in severe cases of typhoid fever, especially if the patients are undernourished. Furthermore, the products of the putrefaction of meat in the intestine may not only give rise to digestive disorders, but may irritate the kidneys during their excretion and produce albuminuria. Meat extracts, such as beef juice and bouillon, have often been recommended, and sometimes have constituted the sole article of the typhoid diet. While the use of small quantities of these preparations may be advantageous at times to stimulate the appetite, two objections may be raised to them—the small amount of energy they furnish and the high percentage of extractives they contain. Beef juice as ordinarily prepared furnishes 25 calories to each 100 c.c. (3 ounces); bouillon furnishes only 8. The extractives in beef juice and in bouillon average about 2 per cent. Beyond stimulating the appetite, they serve no useful purpose, and may prove toxic.

Since meat and meat preparations are not necessary in order to supply the typhoid fever patient with nitrogen, the objections which have been raised to them render it advisable that they be excluded from the diet or at least that they be given with caution.

Eggs. Egg albumin water has been used extensively in the treatment of typhoid fever. White of egg, shaken up with ice, flavored with lemon or sherry and sugar, and strained, has also been recommended. But the value of whole eggs has apparently been overlooked, though they have been employed extensively in other febrile diseases, as, for example, in septic diseases and tuberculosis. Aufrecht and Simon[7] have shown that lightly boiled and raw eggs have a higher food value as part of a mixed diet than a corresponding amount of meat, and that lightly boiled eggs are slightly more digestible than raw eggs. The digestibility of boiled eggs is somewhat lowered by the addition of butter.

Patients with typhoid fever take readily and digest from four to six eggs a day. Eggs may be used to supply not only nitrogen, but energy. Six eggs, for example, furnish about 7 grams of nitrogen and 480 calories.

Fats. The most suitable forms of fat for the typhoid fever diet are cream, butter, and yolk of egg. The principal objections to fat are that it may cause nausea, vomiting, other digestive disturbances, and diarrhea. I shall not enter here into a discussion of the disputed question whether fat is capable of causing disturbances of metabolism. It will only be necessary to say that there has been no evidence in any of the cases of this series of such disturbances, though many of them took large amounts of fat.

The tolerance for fat in typhoid fever is much greater than has been supposed. I have often given as much as 200 to 250 grams

[7] Deutsch med. Woch., 1908, xxxiv, 2308.

of fat a day without producing disturbances of any kind. Yet fat has shown a tendency to cause nausea and vomiting and diarrhea when the quantity has been carried too high. These symptoms, however, have always subsided promptly when the fat was diminished or stopped. Patients differ in their behavior toward fat, and the fat tolerance must be determined in each case.

Milk. Milk has been used probably more than any other food in the treatment of typhoid fever, yet few subjects provoke more discussion in medical assemblages than the value of milk in this disease. Many persons declare they cannot take milk even in health. Many physicians believe that milk always produces digestive disturbances and tympanites in typhoid fever. The majority of typhoid fever patients taking the milk diet grow very tired of it before they are permitted to have other food. This, however, is an argument not so much against milk as against the practice of limiting the patient to one article of food.

Milk is an important, but not essential, constituent of the high calory diet. Because of its importance, the value of milk and the arguments against it must be considered at some length. Van Noorden[8] states that the idea which many people have that they cannot take milk is "purely imagination; . . . there are almost no people who do not bear milk well or who cannot accustom themselves to its use." Peabody,[9] in an article protesting against milk as an exclusive diet in typhoid fever, says: "Milk will always remain the most serviceable general food in disease, and especially in fever, largely because it is swallowed with much less effort than attends the taking of other foods . . . and because it is so commonly well borne." Pavlov[10] states that "milk causes a secretion both from the stomach and pancreas; . . . milk excites not only a really effective, but also a very economic secretion; . . . a much larger fraction of its nitrogen is free for use by the organism than with any other kind of food. How admirably, therefore, the food prepared by nature subserves its purpose when compared with all others."

In rare instances, however, persons exhibit a definite idiosyncrasy against milk. Halberstadt[11] considers the idiosyncrasy to be a symptom of a congenital constitutional anomaly, comparable to anaphylaxis. The idiosyncrasy may be against the albumin, fat, or whey. In some instances the deleterious effects of milk are thought to be due to a change it causes in the flora of the intestine. Definite poisoning occurs in these cases, often with inflammatory changes in the alimentary tract, and they must not be confounded with patients in whom, it is claimed, digestive disturbances and

[8] Twentieth Century Practice, vol. ii, p. 153.
[9] New York Med. Record, 1892, xlii, 620.
[10] The Work of the Digestive Glands, 2d English edition, 1910, p. 229.
[11] Arch. f. Kinderheilk., 1911, lv.

tympanites occur from the use of milk. Tugendreich[12] has described a similar poisoning by buttermilk under the title of "buttermilk fever."

With regard to the statement that milk always produces digestive disturbances and tympanites in typhoid fever, each physician will probably be guided by his own experience. There is no inherent reason why milk should be more indigestible in typhoid than in any other fever. My experience is in favor of milk. For years before the development of the high calory diet I gave milk exclusively to patients suffering from the disease. Since 1907 milk has formed an important part of the diet. Yet it is a familiar fact that there is a limit to the quantity of milk which patients can digest. When this limit is overstepped, the bulk of the stools increases, milk curds appear, and diarrhea and tympanites may occur. But, to say that a patient cannot take milk because excessive quantities cause alimentary disturbances is not a well-considered argument. In addition to the fear of causing such disturbances, excessive quantities should be avoided, for the reason that the total potential energy of the milk is not utilized, as is shown by the waste in the stools.

What quantity of milk is to be considered excessive can be determined only by the ability of the individual patient to digest it. This ability probably varies under different conditions. In my experience the average patient with typhoid fever is able to digest 1½ to 2 quarts of milk a day without difficulty.

The argument that milk favors the growth of the typhoid bacillus in the intestine is largely theoretical, and is based upon the discarded conception that typhoid fever is an intestinal disease.

While milk is not an essential constituent of the high calory diet—no one article of food is—it will be found difficult to supply a patient with sufficient energy on a milk-free diet without unduly disturbing the protein, fat, and carbohydrate ratios. But after all has been said, the quantity of milk in the diet must be arranged according to the tolerance of the patient for it. If it is known to produce digestive disturbances, it should be peptonized, or the quantity be diminished, or it should be stopped altogether.

Carbohydrates. The carbohydrate supply may be obtained from the starches or sugars, or both.

Starches. Only such starchy foods should be selected as are easily digested and contain no cellulose. Foods with a low percentage of water are to be preferred, as otherwise their bulk is objectionable. Crackers and toast are especially valuable. Well-boiled cereals (without cellulose), rice, and baked or mashed potato may be given in moderation for sake of variety. The only objection to starchy foods in typhoid fever is their bulk.

[12] Deutsch. med. Woch., 1909, xxxv², 2319.

Sugars. In order to meet the carbohydrate demands of the patient, one or more of the sugars must be employed. For practical reasons the choice lies between cane-sugar, lactose, and glucose. Cane-sugar is so sweet that it soon palls upon the taste when given in quantity. Opinions differ as to whether it ferments readily in the intestine. Jacobi[13] states that it ferments less easily than lactose in the case of children. Adults probably differ in their ability to handle it. I have given a tablespoonful at a time in coffee, lemonade, etc., and should not hesitate to increase this amount cautiously. Glucose, because of its taste, likewise soon palls upon the senses. It has not been given to any of the cases of this series.

An impression prevails that lactose does not ferment readily in the intestine, though I have not been able to find the investigations upon which this opinion rests. The typhoid bacillus is not capable of fermenting lactose. In my experience it is not fermented readily in typhoid fever by other organisms than the typhoid bacillus, nor has it exhibited the laxative properties which have been attributed to it. Lactose is not very sweet and does not pall quickly upon the taste. Halasz[14] found that persons in health are able to take 150 grams of lactose at a time without the production of glycosuria, while persons suffering from dilatation or tumors of the stomach were able to take only 120 grams. Bauer[15] found the tolerance for lactose in cirrhosis of the liver to be 80 to 100 grams. I have never given more than 140 grams at a time. In no case of the series, whose urine was examined repeatedly (the urine of about 25 of the cases was examined daily), did glycosuria occur.

It should be added that Langstein[16] is of the opinion that lactose, of all the carbohydrates, is least adapted to the child whose nutrition is disturbed, and that cane-sugar is more valuable. Howland tells me that he has found it difficult to give the high calory diet, as here outlined, to young children. Kerr,[17] on the other hand, recommends the diet. As no patient of this series was under twelve years of age, I have formed no opinion.

Fruits. Lemonade, orange juice and orangeade, and apple-sauce have been given to many patients of this series. There has been no reason to think that these fruits have disagreed with them. Fruit has not been permitted, however, or has been given in small quantity and with caution, when patients were suffering from diarrhea.

The foods which have been mentioned above are the only ones which have been employed to a sufficient extent to justify their

[13] Personal communication.
[14] Deutsch. med. Woch, 1908, xxxiv, 818.
[15] Wien. med. Woch., 1906, lvi, 20, 2537.
[16] Jour. Amer. Med. Assoc. (Berlin letter), 1910, lv, 1823.
[17] Amer. Jour. Obstetrics, 1909, lx, 1064.

recommendation, but the diet will unquestionably admit of further elaboration, especially in the matter of variety.

Proprietary Foods. A great variety of proprietary foods are manufactured. They may be roughly classified as meat extracts, other protein foods, some of which have been partially predigested, and foods which have been reënforced by the addition of carbohydrate or fat, or both. They are marketed as liquids, pastes, and powders. The protein foods are made from meat, eggs, milk, blood, plants, malt, and of mixtures of these. The sources of these foods suggest that their native ingredients may be equally valuable.

Concerning meat extracts, Bigelow and Cook[18] state that "meat juice prepared in the home or hospital . . . is far superior as a food to the commercial meat extracts and so-called meat juices." Many of the liquid preparations contain alcohol—some as much as 20 per cent.—which fact must be borne in mind or an excessive quantity of this drug may be administered. The so-called predigested protein foods must likewise be given with caution, since it has been shown that proteoses and peptones may cause diarrhea and other digestive disorders. The work of Ewing and Wolf, as already mentioned, has demonstrated the danger of giving protein to patients who take other foods poorly, and the frequently advertised advice to give such patients proprietary protein foods must be unreservedly condemned.

Lusk[19] states that "the principal value of 'patent' foods lies in their flavor. . . . That beef, milk, cream, butter, and rice are equally suitable for all the purposes of proper living is a fact not sufficiently advertised."

If it should become necessary in any case of typhoid fever to give a patient an artificial food, a preparation in which carbohydrate predominates should be selected, and its fuel value should be clearly understood.

In my experience proprietary foods are unnecessary in the treatment of typhoid fever. I have always found that, if a patient could take food at all, he could take a natural food.

Argument for the High Calory Diet. The value of the high calory diet must rest ultimately upon the results obtained from its use in a large number of cases. Pending this verdict, estimates of its value may be made from such sources as are available. These sources comprise our knowledge of nutrition, of bacterial infections in general, and the opinions of physicians of experience in the treatment of typhoid fever.

It is axiomatic that life cannot continue unless the body is supplied with energy for its metabolic exchanges. If food is not available in sufficient quantity, the tissues of the body will be

[18] United States Dept. Agriculture Bull., No. 114, 1908.
[19] The Science of Nutrition, first edition, p. 119.

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drawn upon. Clinical evidence as well as numerous experimental investigations have shown this to be true in fever as well as in health. There is probably no infective disease, except those which affect the alimentary tract locally, which is benefited by partial or complete starvation.

Though typhoid fever often strikes down persons in apparently perfect health, it is generally accepted as true that both the lower animals and men who are undernourished are less able to resist bacterial invasion. Furthermore, healthy laboratory animals furnish a better immune serum than those which are sickly, and the belief prevails that patients suffering from many, if not all, infective diseases are more likely to recover when properly nourished. When in addition we consider that, as Grafe has shown, metabolism in typhoid fever probably follows normal laws, there is no known reason why patients suffering from this disease should be partially starved. On the contrary, and especially in view of the increased metabolism in fevers, all indications point to the desirability, if not necessity, of supplying patients with all the food they require.

Physicians who have raised the nutritive values of their diets are practically unanimous in their opinions as to the beneficial effects of the change. Graves[20] believed that even his meagre diet modified favorably the course of the disease as he knew it. Trousseau[21] shared this belief. In advocating the milk diet, Flint[22] compared the typhoid fever patient to a person in danger of drowning, and said: "As a person in this situation requires only to be buoyed up by some support, so the fever patient in a similar emergency may need only supporting means to live until the disease ends."

Marsden[23] claimed that his patients recovered more rapidly, and that the tendency to asthenic complications was lessened.

Barrs[24] thinks that the sooner a patient returns to a natural diet the sooner will his nutrition be such as to place his intestine under the best possible condition for healing; that free feeding is likely to modify favorably the death rate, to shorten convalescence, and to diminish the risks of complications and sequelæ.

Kinnicutt[25] found, in an analysis of 600 cases on liberal diets, that hemorrhage and perforation were less frequent than on a restricted diet, chiefly milk, and that relapses were not increased.

Many other favorable opinions could be cited, but it seems unnecessary. It is a significant fact that the adverse criticisms of the liberal diets have come for the most part from physicians who have not employed them. Few or no physicians who have given these diets an extended trial have returned to the older restricted methods of feeding. If one accepts the foregoing evidence, the

[20] Clinical Medicine, New Sydenham Society, 1884, i, 136.
[21] Clinique Médicale, 4th ed., i, 350.
[22] Pract. of Med., 6th ed., p. 982.
[23] London Lancet, 1900, i, 90.
[24] Brit. Med. Jour., 1897, i, 125.
[25] Bost. Med. and Surg. Jour., 1906, clv, i.

high calory diet is deprived of the radicalism which has been attributed to it, the object of the diet being simply to supply patients with all the food they need, instead of supplying them with part of it.

Criticisms of the High Calory Diet. The only criticisms which have been made of the high calory diet, so far as I am aware, relate to the ability of the patient to digest and absorb the amount of food recommended.

Von Hoesslin[26] proved that digestion in typhoid fever is only slightly below normal, not more than 10 to 15 per cent.

Eugene F. Du Bois has investigated during the last year the food losses in the stools of several cases of this series. The results will be published in full by him later on, but a brief summary of them may be given here.

The protein losses, with patients taking from 65 to 118 grams, were usually under 10 per cent. The loss in a normal man on the same diet, studied as a control, was 7.9 per cent.

The fat loss in the second week of the disease, when the temperature was high, with patients taking from 147 to 200 grams, averaged 8.84 per cent. The loss in the steep-curve period of the third and fourth weeks, with the patients taking from 150 to 258 grams daily, was 4.15 per cent. The fat loss in the control, taking 164 grams daily, was 2 per cent. According to Rubner, a normal man taking 79.9 grams of fat a day in milk lost 7.1 per cent. in the stools, and a normal man taking 214 grams of fat in the form of butter lost 2.7 per cent.

The carbohydrate loss in all periods of the disease, with patients taking from 215 to 567 grams daily, was only 0.1 to 0.3 per cent. The loss in the control while taking 249 grams was 0.1 per cent.

The results obtained by Du Bois demonstrate that the ability of the typhoid fever patient to digest and absorb the high calory diet is remarkable, and they may be interpreted as an additional indication of the patient's need for such surprisingly large amounts of food. These results should not be interpreted to mean, however, that the typhoid fever patient may be fed indiscriminately with foods which may be taken by the healthy man with impunity, but simply that carefully selected, easily digested foods may be given to typhoid fever patients (in quantities proportioned to the ability of the patients to digest them) without fear of harm.

The further fact should be noted (and this has been observed by all persons who have been brought in contact with the patients), that the stools of patients on the high calory diet presented an unusually normal appearance.

Administration of the Diet. A false impression exists concerning the high calory diet, namely, that a patient should be

[26] Virchow's Archiv, 1882, lxxxix.

given large amounts of food, especially milk sugar, simply because he has typhoid fever, irrespective of the result produced. The physician should endeavor to maintain nutrition in all cases, but I would emphasize the statement that *no patient should be given more food than he is capable of digesting and absorbing.* If the food is vomited or passes through the intestine unabsorbed, the very object of the diet, improvement of the patient's nutrition, is defeated.

In no case can we do more than attempt to give patients the amount of food they require. Failure to accomplish this may depend either upon lack of proper attention to detail on the part of the physician or to lack of coöperation on the part of the nurse, as well as to obstacles which the disease itself interposes. The physician should possess at least a rudimentary knowledge of the calory values of foods. But probably the chief requisite to the successful administration of the diet is intelligent coöperation on the part of the nurse. When a nurse is trained in the use of the diet, general directions regarding the total number of calories and the protein, fat, and carbohydrate ratios will suffice. At her discretion she will increase or diminish the total amount of food, or of particular articles, until further instructions. When a nurse is not trained in the use of the diet, the physician himself must assume immediate control of the feeding.

Cautions in Giving the Diet. Whenever the administration of the high calory diet is undertaken, careful attention should be paid to the behavior of the stomach, the condition of the abdomen, and the number and character of the stools. If any article of food causes persistent disturbances of digestion, it should be diminished in quantity or stopped. The qualification "persistent" is made because neither occasional vomiting, slight tympanites, or mild diarrhea has been found to be a contraindication to the diet.

One should proceed cautiously in all cases in increasing the amount of food, but not necessarily slowly. If for any reason a patient takes all food poorly, as in cases with alcoholic or other gastritis, the diet should be reduced to the simplest terms, but the patient should be given all the food he can take. For reasons already stated, such patients should not be fed exclusively upon meat broths or other preparations in which protein predominates. Attention should be directed to the fact that it is not uncommon for patients on the high calory diet to have several formed stools a day. This, of course, is not an indication to modify the diet. Many patients who, while taking the high calory diet, have only one stool a day will have from three to six stools a day when put upon the "regular" hospital diet containing meat and vegetables.

Milk sugar may cause nausea and vomiting, especially at first, if the quantity is increased too rapidly. I have found, however, only a limited number of patients whose stomachs could not be

educated to tolerate it, even in large quantities. When milk sugar causes nausea or occasional vomiting, it is necessary to diminish the quantity or to change the method of its administration. If it causes persistent nausea and vomiting, it should be stopped, but may be begun again in a day or two in smaller amounts. The addition of only a teaspoonful to milk or other suitable articles of food is just so much energy gained. A similar course should be pursued if the milk sugar causes tympanites, though at times, when this has been slight, I have diminished but not stopped it.

Cream may cause gastric disturbances or diarrhea. In the former case it should be stopped; in the latter, diminution of the quantity may be sufficient to bring the diarrhea under control. I have not considered it necessary to modify the diet when patients were having only two or three diarrheal stools a day. Not infrequently patients entering the hospital with diarrhea have had this stop under the cautious administration of the diet.

The Amount of Food. As has already been pointed out, the amount of food which a patient requires must be determined by *his individual needs.* The calculated requirement serves only as a general indication of them. The condition of the patients of this series, in whom the nitrogen balance was determined, corresponded in general with the amount of nitrogen lost. Patients losing nitrogen lost weight, and the more nearly nitrogen equilibrium could be maintained, the better was the condition of the patient. But since it is manifestly impossible to determine the nitrogen balance, except in a few cases, clinical guides to the patients' needs must be sought. Two such guides have been found useful—the *weight* of the patient, and the state of his *appetite.* It is not practicable to weigh patients in private practice, and the physician must depend upon his judgment to tell whether a patient is gaining or losing in weight. A patient who is losing weight is evidently drawing upon his own tissues, and certainly requires more food.

If hunger has any significance, we must believe that it indicates the need of food. I always try to appease the appetite of a patient who is hungry.

In the earlier stages of the disease, when the temperature is continuously high, it is always difficult and sometimes impossible to give patients the amount of food they require, that is, the amount which will prevent loss of weight. In perhaps the majority of severe cases it will not be possible to give more than 3000 calories, but as the temperature passes into the steep-curve period, the number of calories may gradually be increased. In this period and in convalescence patients take eagerly from 4000 to 6000 calories a day (one patient took 7400 calories). The question of the advisability of permitting patients to have such large amounts

of food has been raised by physicians and others who have seen the cases. In every instance these quantities have been reached only in response to requests from the patients for more food. Some patients have complained of hunger while taking 3500 to 4000, and even more, calories a day, and I have seen no reason for attempting to curb their appetites. It is not likely that all this food is used for producing energy. Part of it is probably stored as glycogen and fat. As will be pointed out later, gains of a pound a day in weight are not uncommon in the steep-curve period and in convalescence. If only half of such a gain is represented by fat, approximately 2000 of the calories would be accounted for, leaving not much more of the potential energy of the diet than is generally conceded to be necessary for the daily expenditures of the patient. Not infrequently patients who have lost flesh during the more active stages of the disease will regain their weight before the temperature reaches normal.

The question of what weight we shall permit the patient to reach presents itself during convalescence in nearly all cases. I have no definite opinion to express upon this question, but because of the after-tendency to obesity in many instances, I have usually followed the practice of changing or limiting the patient's food when the normal weight has been attained. So far as my information goes, the high calory diet does not predispose to obesity after the fever.

Details of Administration. The successful administration of the high calory diet depends upon unremitting attention to detail. It is a good plan to make a frank statement to the patient regarding the object of the diet whenever, in the opinion of the physician, this can be done. However, it is not always wise to enter too fully into particulars. Very often I tell patients that the more they eat, the sooner they will get well, and the effect of the suggestion upon the quantity of food which they will take is sometimes surprising. I tell every patient who is capable of appreciating the advice, to ask the nurse for more food if he wants it, and I tell the nurse to give the patient all the food he can digest and absorb.

Typhoid fever patients cannot all be fed alike. Their preferences for and idiosyncrasies to foods are not removed by the fever. Yet often the judicious substitution of one article of food or dish for another will increase the fuel value of the diet by several hundred calories. Sometimes patients who complain that the milk is too sweet when it contains one-half to one ounce of milk sugar will take eagerly from two to four ounces of milk sugar in custard, ice cream, or lemonade. As in every other illness, the physician should permit as great variety of foods as is consistent with the patient's wellbeing.

Ordinarily, when a patient first comes under observation he is put upon plain milk for a day or two. The subsequent procedure

depends upon the patient's condition; that is, whether he is suffering from a mild or severe attack of the disease. In the former case he may be allowed foods which require mastication; in the latter, the diet should be liquid.

FOODS AND THEIR CALORY VALUES.[27] All of the foods and recipes which follow have been given thorough trial, and are recommended with confidence for appropriate cases.

Name.	Amount.	Calories.
Apple sauce	1 ounce	30
Bread	Average slice (33 grams)	80
Butter	1 pat ($\frac{1}{2}$ ounce)	80
Cereal (cooked)	1 heaping tablespoonful ($1\frac{1}{2}$ ounces)	50
Crackers	1 ounce	114
Cream (20 per cent.)	1 ounce	60
Egg	1 (2 ounces)	80
Egg, white	1	30
Egg, yolk	1	50
Lactose	1 tablespoonful (9 grams)	36
Milk (whole)	(1 pint 350) 1 ounce	20
Potato (whole)	1 medium	90
Potato (mashed)	1 tablespoonful	70
Rice (boiled)	1 tablespoonful	60
Sugar, cane	1 lump	16
Sugar, milk[28]	1 tablespoonful (9 grams)	36
Toast	Average slice	80

Rubner's figures for calculating the calory values of the different foodstuffs will be found useful: 1 gram pure protein furnishes 4.1 calories; 1 gram pure carbohydrate furnishes 4.1 calories; 1 gram pure fat furnishes 9.3 calories. Nitrogen multiplied by 6.25 equals protein.

FOOD COMBINATIONS AND RECIPES. For the convenience of those desiring to use the high calory diet, the following combinations of foods are given. They are most useful in the early stages of the disease, or in the case of patients who are unable to take solid food.

For 1000 calories a day:	Calories.
Milk, 1 quart (1000 c.c.)	700
Cream, $1\frac{2}{3}$ ounces (50 c.c.)	100
Lactose, $1\frac{2}{3}$ ounces (50 grams)	200
This furnishes 8 feedings, each containing:	
Milk, 4 ounces	80
Cream, 2 drams	15
Lactose, 6 grams	24

[27] The calory values given in the table are approximate, for the most part, but are sufficiently accurate for practical purposes. The values stated are based upon the tables of Atwater and Bryant, Schall and Heisler, Arnold's Diet Charts, and upon weights taken in the hospital.

[28] For practical purposes, the milk sugar may be measured in a medicine glass. Each measured ounce equals 18 grams in weight. If milk sugar is added to water in the proportion of 24 grams to 30 c.c. and the water brought to the boiling point, the milk sugar is completely dissolved. Such a solution, made daily or just before use, will be found convenient in administering the diet.

	Calories.
For 1500 calories a day:	
Milk, 1½ quarts (1500 c.c.)	1000
Cream, 1⅞ ounces	100
Lactose, 3½ ounces (100 grams)	400
This furnishes 6 feedings, each containing:	
Milk, 8 ounces	160
Cream, 2 drams	15
Lactose, 16 grams	64
For 2000 calories a day:	
Milk, 1½ quarts	1000
Cream, 8 ounces (240 c.c.)	500
Lactose, 4 ounces (125 grams)	500
This furnishes 7 feedings, each containing:	
Milk, 7 ounces	140
Cream, 1 ounce	60
Lactose, 18 grams	72
For 2500 calories a day:	
Milk, 1½ quarts	1000
Cream, 8 ounces	500
Lactose, 8 ounces (250 grams)	1000
This furnishes 7 feedings, each containing	
Milk, 7 ounces	140
Cream, 1 ounce	60
Lactose, 36 grams[39]	144
For 3000 calories a day:	
Milk, 1½ quarts	1000
Cream, 1 pint (480 c.c.)	1000
Lactose, 8 ounces	1000
This furnishes 8 feedings, each containing:	
Milk, 6 ounces	120
Cream, 2 ounces	120
Lactose, 1 ounce (30 grams)	120
For 3900 calories a day:	
Milk, 1½ quarts	1000
Cream, 1 pint	1000
Lactose, 16 ounces (480 grams)	1900
This furnishes 8 feedings, each containing:	
Milk, 6 ounces	120
Cream, 2 ounces	120
Lactose, 2 ounces	240

When the above combinations are employed, it is generally desirable to add eggs to the diet in order to raise the nitrogen to the desired amount. The eggs may be soft-boiled or be shaken up in any of the above feedings unless distasteful to the patient, though the addition of an egg makes the stronger mixtures very rich. I have given some patients who seemed unable to get enough to eat 4 ounces of milk, 4 ounces of cream, 2 ounces of milk sugar, and an egg at a feeding. Such patients, however, are exceptional.

Milk toast, with the addition of butter or cream, is relished by many patients.

The following menus were arranged by Miss Mary E. Sheehan, head nurse in Ward A1 of Bellevue Hospital, and have been em-

[39] If this and the following combinations are too sweet, a portion of the milk-sugar may be given in some other form.

ployed, with such modifications as individual patients required, for the last two years. They may be followed in general at any stage of the disease if the patient is capable of taking solid and semisolid food, and if he is hungry, but are most useful in the later stages, and in convalescence. The night feedings are given when the patients' temperatures are taken in the course of the ward routine.

The diet for this day furnishes 3910 calories.

	Hours.	Total.	Calories.
Milk, 6 ounces	9 A.M.; 1, 3, 7	1260 c.c.	860
Cream, 2 ounces	10 P.M.; 1, 4	420 c.c.	840
Lactose, 10 grams		70 grams	280
			1980

At 11 A.M.	Calories.
Egg, 1	80
Mashed potota, 20 grams	20
Custard, 4 ounces	250
Toast (or bread), 1 slice	80
Butter, 20 grams	150
Coffee.	
Cream, 2 ounces	120
Lactose, 20 grams	80
	780

At 5 P.M.	Calories.
Egg, 1	80
Cereal, 3 tablespoonfuls	150
Cream, 2 ounces	120
Applesauce, 1 ounce	30
Tea.	
Cream, 3 ounces	180
Lactose, 20 grams	80
	640

At 7 A.M.	Calories.
Egg, 1	80
Toast, 1 slice	80
Butter, 20 grams	150
Coffee.	
Cream, 2 ounces	120
Lactose, 20 grams	80
	510

Milk sugar lemonade may be substituted for the milk mixture at three o'clock.

The diet for this day furnishes 5580 calories.

	Hours.	Total.	Calories.
Milk, 5 ounces	9 A.M.; 11, 1, 3, 7	1200 c.c.	820
Cream, 2 ounces	10 P.M.; 1, 4	720 c.c.	1440
Lactose, 15 grams		120 grams	480
			2740

At 11 A.M.	Calories.
Eggs, 2	160
Toast, 2 slices	160
Butter, 20 grams	150
Mashed potato, 70 grams	70
Custard, 8 ounces	500
	1040

At 5 P.M.	Calories.
Egg, 1	80
Toast, 2 slices	160
Butter, 20 grams	150
Cereal, 6 tablespoonfuls	290
Cream, 4 ounces	240
Applesauce, 1 ounce	30
Tea.	
Cream, 2 ounces	120
Lactose, 20 grams	80
	1150

At 7 A.M.	Calories.
Egg, 1	80
Toast, 2 slices	160
Butter, 20 grams	150
Coffee.	
Cream, 3 ounces	180
Lactose, 20 grams	80
	650

The diet for this day furnishes 5570 calories. The ménu for the hospital "dinner" calls for chicken, and therefore should not be employed until convalescence is well advanced.

	Hours.	Total.	Calories.
Milk, 5 ounces	9 A.M.; 11, 1, 7	1050 c.c.	700
Cream, 3 ounces	10 P.M.; 1, 4	630 c.c.	1260
Lactose, 15 grams		105 grams	420
			2380

At 11 A.M.	Calories.
Eggs, 2	160
Mashed potato, 80 grams	80
Custard, 8 ounces	500
Creamed chicken, 1 ounce	50
Toast, 2 slices	160
Butter, 20 grams	150
	1100

At 5 P.M.	Calories.
Toast, 2 slices	160
Cereal, 6 tablespoonfuls	290
Cream, 2 ounces	120
Lactose, 20 grams	80
	650

At 3 P.M.	Calories.
Lemonade (lactose, 120 grams)	480

At 7 P.M.	Calories.
Egg, 1	80
Cereal, 5 tablespoonfuls	250
Cream, 2 ounces	120
Toast, 2 slices	160
Butter, 20 grams	150
Coffee.	
Cream, 2 ounces	120
Lactose, 20 grams	80
	960

The following recipes were arranged by Miss Edna Cutler, formerly Dietitian to Bellevue Hospital. They were arranged with the double purpose of adding variety to the patient's dietary, and rendering the milk sugar more palatable, thus making it possible to increase the quantity administered. I have tasted most of these dishes, and have found them savory. Any of them may be given to suitable patients at appropriate times.

Cocoa with milk:	Calories.
1 rounding teaspoonful of cocoa	50
2 ounces of milk sugar	240
4 ounces of milk	80
2 ounces of cream	120
	490

Mix the sugar and cocoa; cook in the milk until dissolved. Serve with the cream.

Cocoa:	Calories.
1 heaping teaspoonful of cocoa	50
2 ounces of milk sugar	240
½ cup of water.	
3 ounces of cream	180
	470

Mix the cocoa and sugar, add the water, and boil. Then add the cream, or use less cream and serve with whipped cream.

Coffee:	Calories.
1½ ounces of milk sugar[20]	180
4 to 5 ounces of strong coffee.	
2 ounces of cream	120
	300

Plain junket or rennet custard:	Calories.
25 grams (—1 ounce) of milk sugar	100
5 ounces of milk	100
¼ junket tablet.	
1 ounce of cold water.	
Few drops of vanilla.	
	200

See directions for cocoa junket.

Cocoa junket:	Calories.
1 teaspoonful of cocoa	50
25 grams of milk sugar	100
5 ounces of milk	100
¼ junket tablet dissolved in 1 ounce of cold water.	
	250

Mix the cocoa and sugar, add the milk, and heat *lukewarm*, stirring constantly; add the dissolved junket, stir thoroughly, and leave in a cool place to set.

Soft custard:	Calories.
1 cup of milk (8 ounces)	160
1 egg	80
2 ounces of milk sugar	240
Speck of salt.	
2 to 3 drops of vanilla or	
Caramel made of 3 tablespoonfuls of granulated sugar	20(?)
	500

Beat the egg slightly, add the sugar, salt, and hot milk slowly. Cook in a double boiler, stirring constantly, until it thickens a little (if cooked too long, the custard will curdle, but may become smooth again if set in a dish of cold water and beaten at once). Flavor and cool.

To make caramel: Put the sugar in a pan directly over heat and burn until a very dark brown. Dissolve in hot water or milk.

Baked custard:	Calories.
1⅕ ounces of milk sugar	160
6 ounces of milk	120
1 egg	80
Nutmeg or vanilla.	
Speck of salt.	
	360

Beat the egg slightly. Warm the sugar and milk, stirring constantly, add to the egg, strain into a custard cup, and flavor. Bake in a pan of water in a moderate oven until a knife when cut into it will come out clean (30 minutes to 1 hour).

[20] By previously dissolving the milk sugar in water, 72 grams of it may be put into a cup of coffee.

Bread pudding:	Calories.
1½ ounces of milk sugar	180
6 ounces of milk	120
1 egg	80
1 slice of bread (⅜ inch thick)	60
½ ounce of butter	120
	560

Spread the bread with butter and cut into squares. Beat the egg slightly; heat the milk and sugar, stirring constantly; mix with the egg and pour over the bread. Grate nutmeg over the top, and bake the same as the custard.

Vanilla ice cream:	Calories.
4 ounces of cream	240
2 ounces of milk	40
2 ounces of milk sugar	240
Speck of salt.	
Few drops of vanilla.	
	520

Mix the cream, milk, and sugar, and heat, stirring constantly, until the sugar is dissolved. Then flavor, cool, and freeze.

Lemonade:	Calories.
4 ounces of milk sugar[31]	480
7 ounces of cold water.	
2 tablespoonfuls of lemon juice (or to taste).	

Boil the sugar and water for two minutes, add lemon juice to taste, strain, and cool.

ANALYSIS OF CASES. Conclusions drawn from statistical studies of typhoid fever are apt to be misleading unless the number of cases is large and unless they cover many years. Epidemics differ in severity, and the frequency of complications and relapses varies in different years. Yet the effect of raising the nutritive value of the diet in even a limited number of cases may furnish important evidence of the results to be anticipated in other cases. The fact that metabolism apparently follows normal laws in typhoid fever justifies a comparison of the effects of starvation in this disease with the effects of starvation in health. It is not necessary to starve the race in order to determine that starvation is detrimental. Analogously, if a few typhoid fever patients are benefited by improving their nutrition, the assumption that the majority will be, at least appears probable.

There are 111 cases in the series.

Character of Illness. Thirty-seven of the cases were mild, 43 were severe, and 31 were very severe.

Mortality. Eleven of the 111 cases died, giving a mortality of 10 per cent. The simple statement of the mortality, however, does not convey sufficient information regarding the cases. The mortality rate should be compared with that of cases on other diets in the same epidemics, and the characters of the disease in the cases furnishing the mortality should be considered.

[31] Some patients have said the lemonade as prepared was not sweet enough, at which times 1 or 2 tablespoonfuls of cane sugar have been added.

For purposes of comparison, a table of all cases treated in Bellevue and Allied Hospitals during the period covered by this report is given (there were so few cases on the high calory diet in 1907 that they are not included in the computation).

Year.	B. H. and A. H. Total cases.	Total deaths.	Diet cases. Total.	Deaths.
1907	...	...	9	0
1908	315	55	28	1
1909	258	37	39	3
1910	302	45	35	7
	875	137	102	11 = 10.7 per cent.
	102	11		
	773	126 = 16.5 per cent.		

As will be seen from the table, 16.5 per cent. of all cases in Bellevue and Allied Hospitals in 1908, 1909, and 1910, exclusive of the cases on high calory diet, died, while 10 per cent. of the cases on this diet died.

It seems fair to assume that the type of infection in the different hospitals of the department was essentially the same in the same seasons.

In order that the character of the disease in the cases which died, and their relation to the diet may be appreciated, it will be necessary to give a brief clinical history of each case.

Case I.—Series No. 11, 1908. E. S. Admitted on the tenth day of the disease; died on the thirteenth day; "walking typhoid;" heart in bad condition on admission; patient pale and dyspneic. Diet started on the eleventh day. On the twelfth day intense air hunger developed; the patient's face was drawn and cyanosed; heart sounds were faint, action irregular.

Case II.—Series No. 47, 1909. W. S. Admitted on the seventh day of the disease with lobar pneumonia as a complication; died on the twentieth day. Has used alcohol to excess; became irrational shortly after admission. Temperature ranged up to 106° F. Diet was taken indifferently. Prognosis very grave from day of admission.

Case III.—Series No. 51, 1909. C. McG. The patient had been on a ten-day spree, lasting until the ninth day of the disease; severe diarrhea during the debauch. Admitted on the fourteenth day with alcoholic gastritis and persistent nausea and vomiting. Food was taken indifferently. Perforation occurred on the twentieth day; operation was performed immediately; death on the twenty-fourth day.

Case IV.—Series No. 74, 1909. A. S. Admitted on the eighth day of the disease; died on the fiftieth day. Temperature range high; dropped to normal on the morning of the thirty-fourth day, but evening temperature was never below 101° F.; rose in a few

days to its former high level. Persistent delirium and diarrhea. Developed double otitis media on the twenty-second day. Took food only fairly well.

Case V.—Series No. 77, 1910. J. R. Admitted on the eighteenth day of the disease. Temperature very high; patient delirious. Developed pulmonary edema, and died on the twenty-second day. At autopsy, acute bronchitis, extensive bronchopneumonia, chronic otitis media, and acute parenchymatous nephritis were found as complications.

Case VI.—Series No. 89, 1910. T. K. Very alcoholic on admission; irrational at times. History indefinite, probably in the fourth week of the disease. Persistent nausea and vomiting; unable to take much food. Passed a few small blood clots on the seventh day in hospital; severe hemorrhages on the ninth and tenth days. Complained of pain on right side of abdomen on tenth day; distinct mass palpable below umbilicus. Operation for supposed perforation showed this to be a malformed kidney lying across the brim of the pelvis. The patient had status lymphaticus. At autopsy, acute bronchitis and bronchopneumonia were found as complications.

Case VII.—Series No. 91, 1910. J. S. Admitted on the fifteenth day of the disease. Has status lymphaticus. Patient resisted all treatment, and took very little food. Developed bronchopneumonia about the thirty-seventh day, and died on the thirty-ninth.

Case VIII.—Series No. 92, 1910. T. R. Admitted on the ninth day of the disease; during the day the patient had an intestinal hemorrhage, and pulse became weak. On the following day the patient passed 20 ounces of dark-red blood. Developed diphtheria on the thirteenth day. Died on the twentieth day.

Case IX.—Series No. 93, 1910. J. E. Admitted to surgical ward with abscess of prostate twelve days before the typhoid developed. Temperature fell slowly to normal after operation, but immediately rose again. Transferred to medical ward on the ninth day of the typhoid. Operation wound discharging up to the eighteenth day. Took diet well. Developed lobar pneumonia on the twenty-third day; died on the twenty-sixth.

Case X.—Series No. 94, 1910. A. H. Admitted on the tenth day of the disease. Diet started at once and was taken well. Had severe intestinal hemorrhage on the fourteenth day; blood continued to appear until the twenty-first. On the twenty-second day the temperature dropped to 98° F.; respirations became rapid and shallow; patient died on the twenty-third day. The diet was stopped on the occurrence of the hemorrhages.

Case XI.—Series No. 107, 1910. J. N. Admitted on the eighth day of the disease. Diet started at once; patient was hungry and took food well. The disease ran an unusually long course. Lobar pneumonia developed, and the patient died on the forty-fifth day.

These histories show that Cases IV, X, and XI were the only ones in which the diet had a fair trial. The other cases have not been excluded from the series because similar ones undoubtedly exist among those not on the diet (the details of which have not been accessible), and because of possible bias. If one excludes all deaths except Cases IV, X, and XI, the mortality rate is only 2.7 per cent.

The number of cases in the series and the length of time that the high calory diet has been on trial—four years—apparently justify the assumption that the mortality from typhoid fever may be reduced by maintaining the patient's nutrition at the highest possible level.

Relapses. Relapses occurred in 23 of the 111 cases, or in 20 per cent. The incidence of relapses by years was as follows:

	Cases.	Relapses.	Per cent.
1907	9	2	22
1908	28	10	39
1909	39	9	23
1910	35	2	5
		Average	20

The percentage of relapses in the first three years is so high that information was sought regarding their occurrence on the First Medical Division.[32] The result is as follows:

	Cases.	Relapses.	Per cent.
1907	51	13	25
1908	31	10	32
1909	36	6	16
1910	46	15	32
		Average	26

I do not believe that one is justified in drawing any conclusion from the comparison of these statistics except that the percentage of relapses was high on both the milk and high calory diets among the cases cited. The comparison may indicate, however, that neither the milk nor the high calory diet has any effect upon the incidence of relapses.

Complications. Hemorrhage. The occurrence of hemorrhage in the different years was as follows:

	Cases.		Per cent.
1907	9	1 with hemorrhage	11
1908	28	5 with hemorrhage	17
1909	39	2 with hemorrhage	5
1910	35	4 with hemorrhage	11
		Average	12

[32] I wish to express my thanks to the visiting physicians on this Division for the privilege of using these statistics.

Three cases complicated by hemorrhage died from other causes; 1 case died as the result of hemorrhages.

A striking fact has been observed in the cases complicated by hemorrhage. When the patient has been well nourished, the loss of blood has produced little, if any, more effect than the loss of a corresponding amount of blood would produce in a healthy man.

Other complications. Perforation occurred in 1 case, lobar pneumonia in 6 cases, otitis media (probably the lighting up of an old process in all instances) in 9 cases, bronchopneumonia in 4 cases, cholecystitis in 2 cases, pulmonary tuberculosis in 1 case, tuberculous abscess about rectum in 1 case, pleurisy in 2 cases, diphtheria in 2 cases, phlebitis in 3 cases, periosteitis in 1 case, panophthalmitis in 1 case, and abscess about rectum (non-tuberculous), 1 case.

Weights of Patients. Weights of the patients were taken usually every second or every third day, on a platform constructed for the purpose. The majority of the patients lost some weight during the course of the disease. The losses corresponded in general with the amount of food they were able to take. In the majority of cases the losses were under 10 pounds, and often did not reach 5 pounds. The greatest loss recorded was 20 pounds, between the ninth and twenty-second days of a thirty-one-day case. The attack was mild, though long, and the patient took his food well, reaching 3100 calories on the second day after admission, and 4000 later on. Some patients who lost flesh during the early stages of the disease, recovered it in the steep-curve period. Other patients gained 1 to 2 pounds during the febrile period, and several patients gained in weight during relapses. In some the weight remained stationary.

Gains in weight during the first two weeks of convalescence —when under the method of partial starvation patients usually continue to lose—varied from 3 to 10 pounds. In a few instances temporary losses of 1 to 3 pounds occurred in this period. A number of patients gained 1 pound a day; one gained 3 pounds in two days; one gained 5½ pounds in three days; and one gained 9 pounds in five days.

As the gains in weight were retained by the patients even after the food was changed to the "regular" hospital diet, they may be assumed not to have been due simply to water retention.

The Individual Patient. The claim has been made from time to time that particular diets shorten the course of typhoid fever, but the evidence for such claims will not bear close analysis. No one can predict how long the fever will last in any given case. There is no reason to think that the high calory diet has had any influence upon the duration of the febrile stage of typhoid fever, but there is strong evidence that it modifies the course of the disease favorably. Though perhaps the majority of patients on the diet lose some flesh, the marked emaciation formerly so characteristic of the disease does not occur. Patients often retain their

facial coloring throughout the disease. Mentally they are alert and take an active interest in their environment. Many of them have been permitted to read the daily papers and magazines without injurious effects. The so-called typhoid state has not developed in any patient who was able to take sufficient food, and has disappeared under the influence of the diet when patients have entered the hospital in that condition. I doubt if a physician glancing casually through the wards would be able to pick out the typhoid fever patients.

The patients have been stronger when they were permitted to get out of bed, usually two weeks after the fever subsides, than similar cases were formerly on the exclusive milk diet. They have left the hospital in shorter time and in better condition. While it has been difficult to follow the patients after they left the hospital, the limited information I have been able to obtain leads me to believe that convalescence has been materially shortened.

While I have believed for several years that the principles underlying the employment of the high calory diet in typhoid fever would be found applicable to other acute infective diseases, the value of the diet in such cases has not yet been tested sufficiently, so far as I am aware, to justify more than tentative recommendations. I have given the diet to patients with lobar pneumonia, but the number of cases has been small. Tympanites is so common in severe cases of pneumonia, and the respiratory distress it causes is so serious, that one should take especial care not to increase it through the careless administration of food. In all cases where it can be done safely during the course of the disease, and generally in convalescence from it, I would suggest that the energy value of the diet be increased by the addition of carbohydrates, though not necessarily milk sugar. The high calory diet has been found to be beneficial in the severer respiratory infections which are commonly called influenzal, and from which convalescence is often so slow. It has been employed with satisfaction in some chronic diseases accompanied by impaired nutrition, and there is reason to believe that it would be useful in severe septic infections and in some forms of pulmonary tuberculosis. But, as has been stated, the diet has not yet been thoroughly tested in any disease except typhoid fever.

Conclusions. 1. None of the older diets for typhoid fever furnishes the patient with sufficient energy for his metabolic exchanges. Therefore a patient taking any of these diets is compelled to live in part upon his own tissues.

2. The amount of food which a patient requires can be determined only by his individual needs. The clinical guides to these needs are the weight of the patient and the state of his appetite. A patient who is losing weight should be given more food if he can digest and absorb it. A patient who is hungry should be given

sufficient food to appease his appetite. In the early stage of severe cases it is always difficult to give more than 3000 calories a day; in the steep-curve period and in convalescence, patients take readily from 4000 to 6000 calories a day.

3. If any article of food causes persistent disturbances of digestion, the quantity given should be diminished, or the food should be stopped; otherwise the object of the high calory diet, the maintenance of the patient's nutrition, is defeated. If a patient cannot take all the food he requires, he should be given all he can digest and absorb.

4. Carbohydrates should furnish the greater part of the energy of the diet. The daily protein ration should not be below 62 grams, nor greatly exceed 94 grams. Clinical evidence indicates that a diet rich in fat may be taken by typhoid fever patients with benefit. Fat has furnished in some cases from one-third to one-half of the total energy of the food.

5. In the cases studied, the high calory diet has apparently modified the course of the disease, shortened convalescence, and reduced the mortality.

Finally, I wish to express my indebtedness and my thanks to Dr. Dana for the privilege of studying cases in his service, to Drs. W. Murray Kerr, T. J. Kearns, W. E. Lowthian, T. R. Pooley, Jr., Harold De Wolf, and William Tomkins, House Physicians in different years, for valued assistance, and to Miss Mary E. Sheehan, Head Nurse in Ward A1, for many practical suggestions and for her untiring aid in carrying out the administration of the diet.

MULTIPLE CONGENITAL HEMANGIO-ENDOTHELIOMAS OF THE LIVER.

By Borden S. Veeder, M.D.,

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AND

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(From the McMane's Laboratory of Pathology, University of Pennsylvania.)

The findings at autopsy in this case from the medical service of Dr. Le Boutillier, at St. Christopher's Hospital, Philadelphia, are so uncommon that we feel justified in placing the case on record. The subject was a female infant, aged ten weeks, one of twins, breast-fed. From birth a distention of the abdomen was noted which constantly and rapidly increased; the infant at the same time

became each day weaker. On examination, the liver was found greatly enlarged, extending to the umbilicus and possessing a palpably nodular surface. Otherwise physical examination proved negative. The urine examination and the Wassermann reaction were negative. The temperature was slightly subnormal. In the hospital the child continued to become weaker, and without further symptoms died.

Autopsy was performed on November 3, 1910, a few hours after death, by Drs. Veeder and Austin. The abstract of the protocol from the records of the McMane's Laboratory of Pathology is as follows:

Body of a fairly well-nourished female infant. Slight postmortem rigidity and cadaveric lividity present. Abdomen markedly distended.

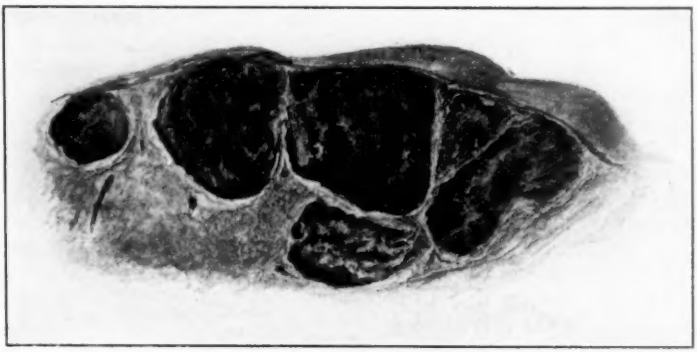
Abdomen. Primary incision showed a thin panniculus adiposus, no bleeding. Peritoneum smooth and glistening. Very slight excess of thin, clear fluid present in the abdominal cavity. No adhesions.

Liver. The liver was greatly enlarged, extending down as far as, and to the left of, the umbilicus, weighed 595 grams, and measured 17 x 9.5 x 6 cm. Its surface showed numerous dark, purplish nodules standing out prominently from the smooth peritoneal covering. These nodules varied in size from that of a pea to that of a horse-chestnut, were slightly umbilicated, and gave the liver an irregular, knotty appearance. Over the dome of the liver 19 of these nodules were counted, and on the under surface, 23. A typical nodule (2 cm. in diameter) had a dark red centre 1.4 cm. in diameter, surrounded by a white translucent zone 1 mm. in width. Outside of this was another dark zone from 1 to 3 mm. in width, apparently due to congestion, with radiations extending from it into the surrounding liver tissue. The nodules were distinctly softer than the surrounding liver substance, and were of about the consistency of brain. On section nodules were found throughout the substance of the liver. They showed, on cut surface, very dark, bluish-red centres, surrounded by a zone of pale white tissue from which branching processes extended inward toward the centre of the nodule. The liver tissue between the nodules was firm, quite yellow, somewhat congested, and showed the lobules faintly demarcated.

Sections of the tumor nodules and liver tissue were embedded and cut in paraffin, and stained with hematoxylin and eosin for microscopic examination.

Microscopic Description. The centres of the tumor nodules are composed of dilated blood spaces, irregularly arranged between numerous narrow trabeculæ of fibrous tissue and atrophic liver cells. The endothelial cells covering the trabeculæ are much more numerous than in the wall of a normal vessel, and in places have proliferated to form a double layer. They have large oval and

somewhat vesicular nuclei, and occasionally show mitotic figures. The blood spaces are densely packed with erythrocytes and a few leukocytes. Around each nodule is an irregular capsule of compressed and fibrosed liver tissue with atrophic and vacuolated liver cells. The capsule of Glisson persists, and shows considerable overgrowth of fibrous tissue, particularly about the bile ducts. At some points the dilated blood channels are apparently dissecting their way into the liver substance, and here a transition can be seen from the normal to the atrophic liver cells. In some places the tumor tissue comes into apposition with the capsule of the liver, while in others a moderate layer of degenerated liver cells and fibrous tissue intervenes. The liver tissue uninvolved by the tumor shows advanced fatty change, the cells being occupied by large vacuoles. The protoplasm stains poorly and is granular. The connective tissue of the parts of the liver uninvolved by the tumor does not show hyperplasia.



Cut surface of liver.

The heart, lungs, thymus, spleen, kidneys, pancreas, adrenals, and abdominal lymph nodes were examined both grossly and microscopically, and no lesions of any moment were found. The only other pathological findings, and apparently they bear no relation to the tumors, were two small ulcerations of the duodenum situated just beyond the pylorus, about 4 mm. in diameter, extending through the mucosa.

From the histological picture the diagnosis of cavernous hemangiomas is evident. The dark centres of the nodules, seen grossly, correspond to the large collections of blood between the newly formed and growing bloodvessel walls. The white encapsulating area corresponds to the surrounding band of fibrous tissue with its atrophic liver cells. The septa passing toward the centre of the nodules from the periphery are bands of overgrown fibrous tissue along the bile ducts and larger bloodvessels.

Angiomas of the liver are not uncommon, but have rarely been reported in infancy or childhood. Primary sarcoma and carcinoma are far more common in childhood, as is shown by the large number of cases which Steffan[1] was able to collect. In searching the literature we have frequently found the statement that angiomas occur often in childhood, but it is seldom that references are given or cases cited, and we are, therefore, inclined to attribute this statement to the assumption by the authors of a congenital origin for the angiomas found in adults rather than to the discovery of the tumor during early life.

Cases of solitary angioma in infants have been reported by Steffan,[2] Michailow,[3] Kaufman,[4] and others, in all, however, less than a dozen.

The number of cases reported of multiple hemangiomas of the liver in children is even smaller. We have, in fact, been able to find but 3. One of these, reported by Chervinsky,[5] in an infant aged six months, is in many respects identical with ours. It was briefly as follows:

A child, born at term, of healthy parents, began to show enlargement of the abdomen a few weeks after birth. This increased, and before death, which occurred at the age of six months, a hard nodular tumor mass was palpable in the upper abdomen. Death occurred apparently from general weakness. There was no family history of syphilis. The autopsy showed the greater part of the abdomen to be occupied by the liver, which weighed 943 grams, and measured 22 x 10 x 6 cm. The liver showed nodules throughout varying in size from that of a pea to that of a hen's egg, deep red in color, and slightly umbilicated. On section the nodules were composed of a dark-red centre surrounded by a white ring, and some showed white fibrous bands running in from the periphery. Microscopically the centres of the nodules were composed of cavities, or spaces, lined by endothelial cells and containing red and white blood cells. The capsule was composed of fibrous tissue and atrophic liver cells, and was somewhat infiltrated with lymphocytes. The parts of the liver distant from the tumor showed some disintegration and an increase of perilobular connective tissue.

A second case, of similar type, occurring in a child, aged seven years (first noticed at the age of five and one-half years), was reported by Sawyer.[6] In this case the family history was negative. The swelling of the abdomen was first noticed about a year and a half before death, and as it increased in size the child became emaciated and developed a slight fever. Autopsy showed no signs of congenital syphilis. Tuberculosis of the spleen, pancreas, and

[1] Geschwülste in Kindersalte, 1905.
[2] Ibid.
[3] Archiv f. Kinderheilk., 1901, xxi, 291.
[4] Spezielle Path. Anat., 1907, p. 579
[5] Archiv. de Phys. norm et Path., 1885, vi, 553.
[6] Rep. Soc. Study Dis. Child, London. 1906, vi, 19.

abdominal lymph nodes was present. The liver weighed about 900 grams, was nodular, and purplish in color. Microscopically, there was, throughout the liver, a widespread, nodular, angiomatous process. Between the nodules there was marked cirrhosis, with broad bands of fibrous tissue intersecting the liver and with prolongations surrounding the lobules. The diagnosis of angiomas with secondary cirrhosis was made.

The third case is described by Bruchanow.[7] It was a case of multiple angiomas of the liver in an infant, aged fifteen weeks, who showed also a number of angiomas of the skin. At autopsy an enlarged liver weighing 710 grams, and measuring 20 x 14 x 6 cm., was found, which contained a number of nodular tumors varying in size from that of a pea to that of a hen's egg. According to Bruchanow, these were true growing, cavernous angiomas. His diagnosis was subsequently attacked by Schmieden,[8] on grounds, however, which do not seem to us to be tenable. These 3 cases are the only ones resembling ours which we have been able to find in the literature.

Several theories have been offered to explain angiomas of the liver. For the majority of cases the old view that the tumor is the result of a capillary dilatation rather than a true blastoma is probably correct. Schmieden[9] and Adami[10] take this stand. Ribbert[11] and Bruchanow[12] explain the capillary dilatation as the result of a developmental defect, the bloodvessels having failed to establish normal relations with the liver cells. Pilliet[13] advocates a theory of fetal inclusion. Probably no one explanation will suffice for all cases. Our own case, as well as the 3 similar ones quoted from the literature, is probably more closely related to the tumors for which Mallory[14] has recently advocated the name "hemangio-endothelioma." These he defines as angiomas which show distinct proliferation of the endothelial cells, the essential cell of the bloodvessel, with distinct new formation of bloodvessels, a true blastoma, therefore. The term was applied by Mallory[15] particularly to those angiomas of the skin, which are not so uncommon, in which there is a true new formation of bloodvessels and which, as a rule, if recurrence is to be prevented, must be removed completely with a considerable portion of the surrounding tissue.

In our case the marked atrophy of the liver cells, the rapid increase in size of the liver, the young character of the fibrous tissue in the nodules, and, above all, the distinct evidence of endothelial cell proliferation, together with the clinical course of the case, all lead us to class the tumors as true blastomas, multiple congenital

[7] Zeitsch. f. Heilk., 1899, xx, 131.
[8] Virchow's Archiv, 1900, clxi, 373.
[9] Loc. cit.
[10] Principles of Pathology, 1908, i, 751.
[11] Virchow's Archiv, 1898, cii, 351.
[12] Loc. cit.
[13] Le prog. méd., 1891, No. 29, p. 50.
[14] Jour. Exper. Med., 1908, x, 575.
[15] Jour. Amer. Med. Assoc., vol. lv, p. 1621.

hemangio-endotheliomas. Specimens of the tissue were submitted to Professor Mallory, of Boston, and to Professors Pearce and Allen J. Smith, of Philadelphia, who have confirmed the diagnosis and to whom we wish to express our thanks.

OBSERVATIONS UPON THE PERSISTENCE OF GONOCOCCI IN THE MALE URETHRA.

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Surely none of us has any precise idea as to how long the gonococcus may survive in the glands that empty into the male urethra; for if they may survive a year or two, who shall deny them a decade? Not I, for one.

And yet I have not seen it. I have never known the gonococcus to survive in a male host for more than three years. I believe I could count upon my ten fingers the instances of a survival of eighteen months or more that have come under my observation. I recollect but one instance in which a year's treatment at my hands failed to free the urethra of gonococci. But I hasten to attribute this result to nature rather than to art. One of the most obstinate cases I ever undertook I treated for six months or more; he still had gonococci. He then deserted all treatment for six months. Then he married, and soon thereafter returned to show me that he was, so far as I could tell, entirely well. To be brief, I believe that the gonococcus does not persist in the male urethra for more than three years, while in at least 90 per cent. of cases it disappears, with or without treatment, within a year.

Upon what is this opinion founded? Not upon the cases and statistics to be cited. These do but illustrate and in some measure confirm my opinion. But this opinion is founded upon a double basis. First, my own inability, in spite of an alert interest in the subject for more than a decade, to find exceptions to the rule; and secondly, the insufficient evidence upon which exceptions are alleged either by physicians who have seen individual patients before they reached my hands, or by those who write.

What, then, is sufficient evidence that the male urethra is or is not free from gonococci?

We may divide the patients who come with this question upon their lips into four classes, as follows:

1. Patients who have apparently been cured at least three months of a gonorrhea and who show (*a*) no purulent shreds or free pus in the morning urine, and (*b*) no pus in the secretion expressed from prostate and vesicles. The observation of the

clinician is sufficient to declare such patients clean without any laboratory confirmation.

2. Patients (usually acute cases) in the same condition, but whose probation of three months has not elapsed. To declare these well the clinician must be fortified by an expert examination for the gonococcus, which should not be made until the patient has remained entirely well without treatment for at least two weeks.

3. Patients (usually with a chronic pearly morning drop) with mild chronic anterior urethritis and perhaps superficial posterior urethritis as well, and who show (*a*) purulent shreds, but (*b*) practically no free pus in the expressed prostatic vesicular secretion. Such patients are usually gonococcus-free, but their clinical diagnosis requires expert laboratory confirmation.

4. Patients with free pus in the urine, which in chronic cases is usually in large part from the prostate or vesicles.

The presence of gonococci in such cases is suggested by the occurrence of complications (acute urethritis, prostatitis, epididymitis, rheumatism, etc.) either spontaneously or as a reaction to local (sounds, injections, sexual intercourse) or general (alcohol, exercise) irritation. Yet such clinical signs have no absolute value in diagnosis, for among the most irritable types of urethritis are certain non-gonococcic ones, while certain urethræ, though still harboring gonococci, are benefited by exercise, alcohol, sexual intercourse, and sounds.

This class of cases, therefore, always requires laboratory diagnosis.

TECHNIQUE OF CLINICAL EXAMINATION.

For the clinical examination the patient partially empties his bladder, submits to a thorough prostatic massage, delivers a drop of the expressed secretion upon a slide, then empties his bladder. The clinician then examines for pus (1) the discharge (if there be any), (2) shreds fished from first urine, (3) centrifuged first urine, (4) expressed prostatovesicular secretion, (5) centrifuged second urine. A few white cells per field do not justify the diagnosis "pus."

I commonly employ the sound, alcohol, and physical exercise in the treatment of chronic urethritis, but not directly for a gonococcus diagnosis. Yet most of my patients have been tried by these irritants in the course of treatment before coming to the final test.

The chief care of the clinician should be not to attempt too accurate a diagnosis. Pus he can readily identify, and from the presence or absence of pus derive inferences accurate up to a certain point. It is in overstepping this limit, in attempting a direct gonococcus diagnosis by the limited means at his command, that he errs.

There is an oft-quoted statement to the effect that the gonococcus may be accurately diagnosticated by the Gram stain[1] in 95 per cent. of cases. What is this "5 per cent." of error? Most of us have attributed it, I fancy, to errors in technique, in preparation and staining of the specimen, etc. But all such sources of error may be eliminated without making the Gram a perfect differentiating stain. There remain an astonishingly large proportion of cases of non-gonorrheal urethritis, the examination of whose pus in smears by a truly expert bacteriologist discloses the presence of bacteria more or less closely resembling the gonococcus. Thus, among the 102 examinations by smear and culture recorded in the tables herewith, made for me by Prof. Elser and Dr. Huntoon, of the Cornell Medical School, 18 showed gonococci (6 of them by smear alone), while 15 showed bacterial forms more or less closely resembling the gonococcus when stained by the Gram method, and required further evidence to identify them precisely.

Pray do not overlook the fact that in one and the same sentence I question the precision of diagnosis by smear alone for 15 cases, and yet grant it accurate for 6 others. For in certain cases the gonococci are so numerous and typical in the smear that even though one fails to cultivate them (for reasons to be discussed later), the diagnosis from such smears may be accepted as entirely adequate.

But, to get back to our original proposition, the clinician does not check up his observations by careful cultures, and to his eye every Gram negative intracellular coccus is a gonococcus. Indeed, many doubtless omit the formality of a Gram stain. Under such circumstances a positive diagnosis of gonococci is justified only in the presence of *both* of two conditions, namely, (1) clinical evidence of gonorrhea, and (2) the presence of numerous, typical gonococci.

These conditions are always fulfilled in cases of uncontrolled acute urethritis, and for the diagnosis of these the clinician need scarcely ever enlist the services of the bacteriologist. But chronic or nearly cured urethritis often fails to present sufficiently clean-cut features to justify a positive or negative diagnosis from the clinician. Indeed, so little faith do I put in my own bacterial

[1] The Gram stain is so frequently carried out in a loose and inaccurate manner that it seems worth while to note the method of staining employed at the Cornell laboratories. It is essential for the success of this stain that the various steps be measured by the watch. The film, after fixation by heat, is treated with an aniline-water, gentian-violet solution for a period of three minutes, blotted and a Lugol solution applied for two minutes. The film is again blotted and washed in absolute alcohol for thirty seconds. In the case of spreads made from exudates, differentiation in absolute alcohol is continued for a longer period, the time allowed depending upon the thickness of the film. As a counter-stain, a very weak watery solution of basic fuchsin is employed, which is allowed to act for thirty seconds. The aniline-water, gentian-violet solution is made up according to the following formula: Aniline water, three parts; absolute alcohol, seven parts; distilled water, ninety parts. This mixture is thoroughly shaken and filtered through a well-moistened filter. To the clear filtrate add 2 grams of Grubler's powdered gentian violet, shake well, and set aside for twenty-four hours. For staining purposes, pipette off the supernatant fluid, which obviates the necessity of filtration. This solution will keep for from four to six weeks, and does not immediately deteriorate, as is popularly supposed. A watery solution of Bismarck brown gives a better counter-stain than the basic fuchsin, unless this is employed in very weak solution to avoid over-stain. Unfortunately, the brown has to be made up fresh.

diagnosis of chronic urethritis that I do not waste time to make more than one examination of a doubtful case. If that is negative, or if the urethritis is apparently cured or non-gonorrheal, I intrust the bacteriological diagnosis to the laboratory.

Such being my point of view, I need pretend no sympathy with the conclusions of those writers who, flying in the face of clinical facts, found a diagnosis of gonorrhea, years after a clinical cure, upon a few Gram-negative intracellular cocci. Indeed, patients upon whom this type of unjustified diagnosis has been made and physicians who put faith in these reports are, as you well know, among the woes of the specialist.

BACTERIOLOGICAL EXAMINATION.

So much for the clinician. The bacteriologist's diagnosis stands upon a totally different basis. By smear and culture he can usually distinguish the bacteria present in the fluids submitted to him. Thus he may err, through his own fault or through the fault of the clinician who submits the specimens to him, and the precision of his diagnosis depends upon a well-prepared specimen as much as upon his own skill. This double point of view is peculiarly important to our understanding of gonococcus diagnosis. A "well prepared" specimen must be fresh, for there is grave probability that gonococci that have remained in cool urine for half an hour cannot be cultivated. Moreover, it must cover the ground, notably the prostate and vesicles.

The technique I at present employ (and have employed in cases 1 to 35 and 67 to 86 of the present series) is the following:

1. Sometimes the patient takes a smear of his morning discharge, but this is usually of little interest.

2. He retains his urine three or four hours, if possible, and then comes to the office, has his glans penis washed with boric acid solution and passes part of his urine (about 100 c.c.) into a large sterile test-tube. This he keeps warm by putting it in his vest pocket when he dons his clothes.

3. I then thoroughly massage the prostate, vesicles, and membranous urethra, and send the patient immediately to the laboratory, where he urinates the material expressed from the internal genital glands into a sterile test-tube. This is promptly centrifuged and examined. All smears are stained by the Gram method. Cultures are made upon ascitic agar streaked with aged human blood serum and upon other media.

By this method the contents of the important posterior urethral glands are not obtained absolutely uncontaminated, yet the admixture of rapidly growing urethral organisms is reduced, and the smears tell quite accurately the preponderance of bacteria in each specimen. In 6 instances gonococci were found in the second

urine passed and not in the first, and 8 times this second urine was sterile while the first urine passed was infected.

But the possibilities of error on the part of the bacteriologist are not exhausted with proper preparation of the specimen. Recognizing that all microscopes are much alike, we are prone to forget that the bacteriologist, the man behind the gun, has as much personality as the physician. Bitter experience has taught us that the very best opinion is the only one worth having.

Yet even the best bacteriological skill may err or may fail to reach a conclusion.

Smears may be inconclusive either because they show: (1) Typical gonococci, but so few in number as not to justify a diagnosis (Cases 46 and 61); (2) bacteria resembling gonococci (Cases 26, 45, 49, 60, 63, etc.); (3) so many bacteria that the bacteriologist fears the gonococci may be concealed by them. Difficulties 1 and 2 are solved by culture or by repeated examination; 3, by local treatment of the urethra to reduce its flora.

Apart from the common laboratory accidents, cultures may fail because they are so overrun with rapidly growing organisms. These may act either by inhibiting the growth of the gonococcus, or by making the isolation of the same impossible.

Whereas the gonococcus was identified 6 times in the smears only (Cases 18, 27, 50, 53, 54, and 59), it was twice (Cases 53 and 55) identified in culture only.

Among the Gram-negative cocci that have been encountered in connection with the human being, the only one that is of interest to us is the Micrococcus catarrhalis. This organism closely resembles the gonococcus in its morphological characteristics, and in its predilection for the interior of leukocytes.

Cultural examination alone, therefore, can differentiate this organism from the gonococcus. The peculiar biochemical properties of this organism have been studied by von Lingelsheim[2] and Elser and Huntoon.[3]

Happily, the Micrococcus catarrhalis is very rarely found in the urethra. I have seen it in only one case (not in this series).

Apart from the Micrococcus catarrhalis it must be emphasized that in a small percentage of cases the normal urethra (and in a somewhat larger percentage the normal vagina) contains Gram negative cocci which, as a rule, can be differentiated from the gonococcus by their form, size and extracellular position. These organisms fail to grow on the usual culture media.

In one case in the present series (Case 72), an organism known as the Diplococcus crassus was encountered. This micrococcus is Gram variable in its reaction, and for this reason its identification is somewhat difficult.

Finally, a rather fruitful source of error remains to be mentioned, namely, degeneration forms of Gram-positive cocci. In examining

[2] Klin. Jahrb., 1906, xv, Heft 2.

[3] Jour. of Med. Research, 1909, xx, No. 4.

films from the urethra stained according to the Gram method, one not infrequently finds organisms which do not retain the dye. The question then arises whether we are dealing with Gram-negative cocci or with altered or degenerated forms of Gram-positive cocci. This question, of course, can only be answered by culture. Such degenerated cocci were found in eleven of my cases.

Thus, even the most competent bacteriological examination may leave the clinician in doubt, for a time at least, and require, if only to save time, laboratory information of another sort.

COMPLEMENT DEVIATION TEST.

Until within the last year we have possessed no such test, but now in the complement deviation test for gonococci devised by Dr. H. J. Schwartz, of Cornell, we have a most excellent means of diagnosis. Since Drs. Swinburne and Schmidt have contributed upon this subject, I need not delay to expound the technique, and shall confine myself to a brief review of my experience with it.

Within its limitations I have found the complement deviation test singularly accurate. But its limitations must be borne in mind. It records the reaction in the blood to an inflammation which is confessedly often very localized and superficial. Consequently we must not expect too much of it in early or mild cases of urethral gonorrhea. On the other hand, if this blood reaction becomes marked, and persists for many months, it may continue positive for an indefinite time after the gonococci have disappeared.

Hence certain rules may be laid down for the interpretation of Dr. Schwartz's test, as follows:

1. A positive reaction in the blood may not be looked for until the gonorrhea has persisted long enough to produce such a reaction. This usually requires about a month.

I have obtained a reaction in twelve days (Case 6), and in another instance a negative reaction after two weeks (Case 21, II).

A gonorrhea controlled from the outset, or chronic and mild, might be expected not to give a blood reaction. Yet such is rarely, if ever, the case. Case 9, a gonorrhea so well controlled by protargol for four weeks that I thought it cured, showed a strong positive blood reaction and gonococci in the prostatic secretion. On the other hand, no case of chronic gonococcic urethritis has failed to give a positive reaction, save one (Case 22), in which a mild gonorrhea of seventeen months' duration gave a + − reaction, followed six and one-half weeks later by a reaction so weak as to be, in Dr. Schwartz's own words, "practically negative." Yet eight weeks later, without confessed or apparent reinfection, the reaction was strongly positive and gonococci were found.

2. A chronic gonorrhea, especially if severe, may or may not leave a persistent reaction for a period of weeks or months, the limitations of which have not yet been determined.

Dr. Schwartz estimates six weeks as an average maximum allowance. Yet I have seen two striking and authentic instances of blood reaction persistent for months.

The first (Case 10) was a most virulent initial gonorrhea of eleven months' duration, during many months of which time the patient was practically confined to the house by subacute pyelonephritis. This patient was free of pus and apparently cured in May, 1910. Prof. Elser at that time could find no gonococci. Yet seven months later the complement deviation reaction was strongly positive, and two months thereafter negative, the patient having taken no treatment and manifested no evidence of disease throughout this time.

Case 25 consulted me for persistent relapsing urethritis. Prof. Elser was unable to find gonococci, and I, attributing his troubles to prostatitis, relieved him by a brief course of prostatic massage. Yet Dr. Schwartz obtained a positive reaction and repeated this two months later, though the patient had been without symptoms or treatment all this while. Six weeks later, however, the complement deviation reaction was negative.

Hence dependence upon the complement deviation reaction exposes one to the possibility of delaying the guarantee of cure for several months. Yet occasionally, as in the cases above cited, clinical and bacteriological evidence may combine to warrant the assurance of a cure before the blood becomes negative. Otherwise one must wait.

But if the complement deviation test is so accurate, may we not substitute it for the bacteriological examination? It were premature to answer this question in the light of our present experience.

The complement deviation test has been proved wrong in 1 examination (Case 8) out of 47; the bacterial test once (Case 15) in over 100 examinations. For brief gonorrheas successfully treated by the repressive (commonly called abortive) injections one must depend chiefly upon the bacteriologist; for all others it is safest to employ both.

But the complement deviation test opens up new possibilities for solving medicolegal problems. Let me cite an example:

Case 21 was a married man who had acquired a gonorrhea several months previously, and had infected his wife. No gonococci were found in the urine, and he was declared free from infection, although his urethritis was not cured. His wife was also examined and pronounced cured. No blood test was made upon either. Yet six months later he returned, denying extramarital exposure, but showing a fresh gonorrhea two weeks old. Both he and his wife immediately submitted to the complement deviation test, and both were negative. Four weeks later he was positive and she negative, while she remained clinically clean. This development of a positive reaction in him showed his infection to be a fresh one due to extramarital exposure, in spite of his fervent denials.

TABLE I.—Diagnosis by Blood Examination.

Case No.	Number of gonorrheal infections and duration of present attack.	Clinical condition and date of subsequent examinations.	Blood.	Bacteria.
1	?, 3 months.	P. G. U.[a]	+	Strepto. and Gram neg. bac.
2	I, 2½ weeks	Well; 1 week.	—	No gonococci.
		2 weeks later.	0	No gonococci.
		4 weeks later.	0	No gonococci.
3	I, brief.	Cured; 4 yrs. Stricture.	—	No examination.
4	I, 18 months.	Well; 18 months.	—	Gram neg. cocco bacilli (colon?). Few strepto.
5	III, ?	Cured; 7 years. Simple urethritis.	—	No examination.
6	I, 12 days.	Cured.	+ —	
		4 weeks later.	+ —	Proteus, staph. and streptococci.
		12 weeks later.	—	
7	?	Stricture; 7 years.	—	No examination.
8	I. brief.	Well a year.	+	Staph. aureus and albus.
		8 weeks later.	—	
		12 weeks later.	0	Strepto. and Staph. albus.
9	II, 4 weeks.	Cured; pus in prostate.	+ +	I, Staph. albus; II, gonococcus.
		1 week later.	0	Same as above.
		3½ weeks later.	0	II, staph., degenerated forms.
		4 weeks later.	0	Streptococci.
		1 week later.	0	II, streptococci.
		4 months later.	—	
10	I, 11 months.	Just well.	0	Staph. and pseudodiphth. bac.
		7 months later.	+ +	
		2 months later.	—	
11	I, brief.	Well; 3 years.	—	I, Staph. albus and pseudodiphth. bac.
		Pus in prostate.	0	II, same and small Gram neg. bac., degeneration forms in films.
12	I, 6 weeks.	Cured.	—	No examination.
13	III, brief.	Cured; 3 months.	—	Staph. albus and strepto.
14	II, 1 year.	Probable P. G. U.	+	Staph. albus and strepto.
		3½ weeks later.	0	Sterile.
		4 weeks later.	+ —	
15	II, 5 years.	P. G. U.	0	I, Staph. albus and pseudodiphth. bac. II, same and gonococci.
		1 week later.	0	Staph. albus; II, sterile.
		6 months later.	—	I, pseudodiphth. bac.; gonococci (?); Cultures failed.
		9 weeks later.	—	
16	?, 7 years.	Gonorrhea.	+	
17	I, brief.	Cured; 18 years.	—	Sterile.
18	I, 4 months	Gonorrhea.	0	I, sterile; II, gonococci in smears, pseudodiphth. bac.
		5 weeks later, cured.	—	II, Staph. albus.
		2 weeks later.	0	II, pseudo-diphth. bac.
19	II, 1 month.	Cured; 18 months.	—	Staph. albus and strepto.
20	?	P. G. U.	—	I, streptococci; II, sterile.
21	I, several months. II, 2 weeks.	P. G. U.	0	I, pseudodiphth. bac.; II, sterile.
		3½ months later.	—	Gonococci.
		4 weeks later.	+	
22	II, 17 months.	P. G. U. (?)	+ —	
		6½ weeks later.	+ —	
		8 weeks later.	+	Gonococci and Staph. albus.
		Later.		No gonococci.
23	I, 10 months.	P. G. U.	—	Staph. albus and strepto.
24	II, 18 months.	P. G. U.	—	
25	Many relapses.	P. G. U.	+ +	I, staph. and pseudodiphth. bac.; II, staph. cultures failed.
		11 days later.	0	II, sterile.
		7 weeks later.	+	
		6 weeks later.	—	
26	II, 3 months.	Gonorrhea.	0	Staph. albus and pseudodiphth. bac., gonococci (?)
		9 months later; P. G. U.	+ —	Same and strepto. and xerosis bac., but probably no gonococci.
		7 weeks later.	+ —	
27	I, several months.	P. G. U.	+ —	Strepto. and pseudodiphth. bac., gonococci in smears only.
28	?, 1 month.	Cured; 6 months.	—	
29	I, 1 year.	P. G. U.	—	
30	I, 15 months.	Cured; 2 months.	—	Bac. capsulatus mucosæ.
31	III, 1 week.	P. G. U.; 10 months.	—	Degeneration forms in plates. Cultures sterile.
32	I, 2 months.	Cured; 1 year.	—	
33	I, 6 months.	Cured; 3 years	—	
34	?, 1 year.	P. G. U.	+	

[a] P. G. U. = postgonorrheal urethritis.

TABLE II.—Diagnosis by Bacterial Examination.

Case No.	Number of gonorrheal infections and duration of present attack.	Clinical condition and date of subsequent examinations.	Bacteria found.
35	II, 2 months.	Cure.	Staph. albus. and strepto.
36	?, 1 year.	P. G. U.	Staph. albus.
37	?, 6 weeks.	Cured. Pus in prostate.	Staph. aureus.
38	II, 3 months.	P. G. U.	Staph. albus and aureus and strepto.
39	I, 2 months.	Cured.	Staph. albus and aureus and strepto., proteus and pseudodiphth. bac.
40	?, 6 weeks.	Cured.	Bac. coli.
41	?, 7 weeks.	Cured.	Staph. albus and strepto.
42	II, 3 weeks.	Cured.	I, staph. albus and aureus; II, Staph. albus.
43	?, 7 weeks.	Cured.	Staph. albus and a small Gram neg. bac.
44	?, 3½ weeks.	Cured.	Strepto. mucosæ.
45	?, 2 months.	Cured.	Staph. albus and strepto., pseudodiphth. bac. and a small Gram neg. extracellular coccus, not morphologically resembling gonococcus.
46	II, 3 weeks.	Cured; stricture.	Strepto., staph. aureus, and pseudodiphth.; on smear one pair of gonococci (?).
		11 weeks later.	I, Staph. albus, strepto., and pseudodiphth. bac.; II, no strepto.; otherwise same.
47	?, 4 months.	Cured.	Staph. albus.
48	?, 2 weeks.	Cured; relapse a week later.	Staph. albus and strepto.
49	II, 7 weeks.	P. G. U.	Staph. albus and gonococci.
		2 weeks later.	Staph. albus and strepto. and pseudodiphth. bac.
50	?, 6 months.	P. G. U.	Bac. coli, staph. and gonococci (in smear).
		1 month later.	Bac. coli., staph.
51	?, 6 months.	Cured.	I, staph. albus, Gram pos. bac.; II, sterile.
52	II, brief.	Cured; 6 years.	Staph. albus, strepto.
53	I, 4 months.	Cured.	Staph. aureus, strepto., Gram pos. bac.
	II, brief.	Cured.	No examination.
	III, 2 months.	Cured.	I, Staph. aureus; II, same and gonococci (in smear).
		3 days later.	Same except that gonococci appear only in cultures.
		18 days later.	I, Staph. aureus and pseudodiphth. bac.; II, staph. aureus, degeneration forms.
54	?, 1 year.	P. G. U.	Staph. aureus, strepto., and gonococci.
		19 days later.	Same; but gonococci only on smears of I.
55	?, 4 months.	P. G. U.	I, Staph. albus; II, Staph. albus and gonococci by culture only.
		1 month later.	II, Staph. albus and strepto.; II, Staph. albus.
56	I, 3 years.	Urethrorrhea.	I, Staph. albus; II, sterile.
57	?, 5 years.	Cured.	Staph. albus, strepto. and pseudodiphth. bac.
58	?, brief.	Cured; 1 year.	I, Strepto., pseudodiphth. bac. and degeneration forms; II, strepto., staph. albus, and degeneration forms.
59	?, 3 months.	Cured; 3 months.	Staph. aureus, strepto., gonococci in smears.
60	I, brief.	Cured; 18 months.	Staph. albus, strepto.
61	I, brief.	Cured, 3 years.	Staph. albus, strepto., and pseudodiphth. bac. In I, by smear, a single-cell containing gonococci. Also degeneration forms.
		7 weeks later.	I, Staph. albus, and pseudodiphth. bac.; II, Staph. albus.
		2 weeks later.	I, Staph. albus., strepto., pseudodiphth. bac.; II, Staph. albus, pseudodiphth. bac.
62	I, brief.	Cured; 6 years.	Staph. albus, strepto.
63	?, 5 years.	Relapsing P. G. U.	I, Staph. albus, strepto., and intracellular degeneration forms (?) in smear. II, Staph. albus.
		11 days later.	Staph. albus.
64	?, 3 years.	P. G. U.	I, Staph. albus; Staph. albus and pseudodiphth. bac.
65	I, brief.	Cured; 10 months.	Staph. albus and strepto.
		1 week later.	Staph. albus.
		17 days later.	Staph. albus, strepto., pseudodiphth. bac.
66	I, Several mos. Well 3 years.	P. G. U.	Staph. albus, strepto.
67	I, well 3 years.	Cured.	Sterile.

TABLE II.—Diagnosis by Bacterial Examination—(*Continued*).

Case No.	Number of gonorrheal infections and duration of present attack.	Clinical condition and date of subsequent examinations.	Bacteria found.
68	II, 3 weeks.	Cured.	Bac. prodigiosus and Gram pos. cocci.
69	?, brief.	Cured; 2 years.	Gram. pos. cocci.
70	?		Staph. albus.
71	I, 6 months.	Cured; 1 month.	Staph.
72	II, 3 months.	Cured.	Staph. albus, diplococcus crassus.
		2 weeks later.	Same.
73	I, 6 months.	Cured; 1 year.	Streptococcus mucosæ.
74	I, brief.	Cured; 3 years.	I, Staph. albus; II, sterile.
75	III, 7 weeks.	Cured.	Staph. albus and Gram pos. bac.
76	?, 8 years.	P. G. U.	Bac. coli. com.
77	I, 2 years.	P. G. U.	Staph. albus and strepto.
78	No gonorrhea.	Simple urethritis.	Pneumococci.
79	I, 1 year.	Gonorrhea.	Staph. albus, gonococci.
		1 month later; cured.	Staph. albus and strepto.
80	I, few weeks.	Well 2 months	Staph. albus, degeneration forms.
81	I, few months.	P. G. U.	Staph. albus, strepto., gonococci, and unidentified bacilli.
		I month later.	Gram. pos. bac.
82	III, 6 weeks.	Cured.	Staph. albus, Gram neg. bac.
83	?		Staph. albus, strepto., degeneration forms.
84	?		Strepto, pseudodiphth. bac.
85	II, 3 months.	Cured; 4 months.	I, Staph. albus, pseudodiphth bac.; II, sterile.
86	I, 3 months.	Cured.	Staph. albus, pseudodiphth. bac.

DURATION OF GONORRHEA.

The tables herewith classify briefly the results of laboratory investigation of 86 patients clinically cured, or nearly cured, of urethral gonorrhea (Cases 21 and 53 twice investigated). Thirty-six were investigated by the complement fixation test, 77 by smear and culture. In 5 instances the patients were believed to be still infectious, and this belief was borne out by the laboratory findings; in 26 the patients had active urethritis, believed to be postgonorrheal (P. G. U.), yet in 8 of them gonococci were found. But among 51 with clinical evidence of cure (only shreds or light haze in urine), only 2 (Cases 9 and 53, III) showed gonococci, both of them brief cases temporarily controlled by repressive injections, while 1 (Case 48) was passed as clean by both clinic and laboratory, yet relapsed, and gonococci were found a week later. The relapse did not appear to be a new infection. Hence I estimate about 4 per cent. of clinical error in cases apparently cured. However, in 10 cases (1, 15, 16, 22, 26, 27, 49, 53, 54, and 59) the clinical presumption of cure was not fully certified by the laboratory findings.

Nevertheless, with all allowance made, I feel justified in stating that in 64 cases gonococci disappeared in less than a year, in 7 others with urethritis, examined from two to eight years after the onset, gonococci were not found, while in 6 (4, 22, 26, 34, 54, and 79) gonococci persisted from one to two years.

In almost all cases these conclusions were verified by clinical

examination of the patient a month or so after the cure had been pronounced. Moreover, I had the opportunity of examining 9 cases cured of gonorrhea from two to eighteen years previously (Cases 3, 5, 11, 17, 33, 52, 62, 69, and 74). In none of them were gonococci found, though the misleading "degeneration" forms of staphylococci appeared in Case 11.

Only twice were gonococci found in cases of urethritis of more than two years' duration. Case 16 had for several years suffered more or less constantly from a urethral discharge, with exacerbations, and with promiscuous cohabitation galore. Gonococci were found and attributed to a recent infection.

Case 15, on the other hand, had a single urethritis five years ago in which frequent examinations by the late Dr. Otis failed to reveal gonococci. He denied having had sexual intercourse with his wife or any one else for the whole five years. He came to me, having consulted no one in the two years since Dr. Otis' death. My clinical examination revealed only a mild chronic urethritis, but Prof. Elser found gonococci, and the patient went home (100 miles from New York), infected his wife, and developed an acute gonorrhea himself. Curiously enough in this case, Prof. Elser made his one error, pronouncing the specimens gonococcus-free[5] on a second examination. But happily before I communicated this report to the patient his new infection had blossomed, and six months later he was apparently back to his mild chronic catarrh, as was his wife, and Prof. Elser declared him probably gonococcus-free. Yet the blood was positive. But nine weeks after this it was negative. My diagnosis of this case is that the patient is an amiable liar.

All of us have encountered cases such as these; we must perforce interpret them as fairly as possible in the light of all other cases. I have never seen one of them that convinced me he had harbored gonococci more than three years.

[5] The laboratory does not guarantee the patient, but only the specimens submitted. Yet with this one exception Prof. Elser has always found gonococci in specimens from patients harboring them.

REVIEWS

ELECTRICITY, MEDICAL AND SURGICAL. By CHARLES S. POTTS, M.D., Professor of Neurology, Medico-Chirurgical College, Philadelphia. Pp. 509; 356 engravings, and 6 colored plates. Philadelphia and New York: Lea & Febiger, 1911.

WHILE claims that are ridiculously absurd have been made by writers on electricity, it is obversely true that of recent years investigations in this department of medicine have revealed a much wider range of usefulness for the electrical current than is generally believed. Dr. Potts is admirably qualified to write on this matter, not alone because of his vast experience in such work, but also by reason of his common sense views on the subject.

In this volume the heretofore separate consideration of the physiological action, the therapeutic uses, and methods of application of each form of current is abandoned, and these subjects are discussed collectively; therapeutic measures are similarly described. In these and in other ways the plan of the work is original, and the author's belief in the value of such methods, which are scientific rather than empirical, is well borne out in the text. This departure, however, would be somewhat confusing if it were not for the generous use of cross references.

The whole subject is comprehensively considered in seven sections, comprising electrophysiology, electrodiagnosis and electroprognosis, general electrotherapeutics, methods of obtaining general and local effects by the indirect action of electricity, and special electrotherapeutics, together with opening and closing collaborate sections on physics and the *x*-rays respectively.

Under electrophysiology is given a very useful chapter in which is summarized the physiological action of the various electrical modalities. In the matter of the sinusoidal current, Kellog receives credit for its early use; this enthusiastic physician is not too abundantly quoted, but perhaps some of his observations on physical therapy need further confirmation.

The important subject of electrodiagnosis is one of the best portions of the volume, and in the actual study of the motor points the reader is aided by the insertion of the invaluable plates from Mosher's *Electrodiagnosis*.

Special electrotherapeutics is given the most space. Here are considered diseases of the nervous system, muscles and joints,

thoracic and abdominal organs, bloodvessels, eye, throat, nose and ear, skin, and the genito-urinary organs, both male and female. A feature of this portion of the work is the illustrating of much special apparatus for use in the application of the current.

Methods of obtaining general and local effects by the indirect action of electricity is a useful section, and vibration is mentioned among other subjects; but we should like to see this given systematic consideration, as is done with heat and light. The more general use of vibration has found expression in the various apparatuses of Zander, and even massage and exercises are given indirectly through the current; abroad numbers of institutions are devoted wholly to such work, and this matter seems worthy of some mention. It is true this part of the volume only deals indirectly with electricity, but the field of physical therapy is not yet given proper consideration in other medical works; therefore we believe the value of this volume would be enhanced by some amplification of this subject.

The electric hot air douche has a distinctive use; it is both palliative and curative, and its application is unattended by pain. We do not see this mentioned, but such an apparatus may be procured, and with it an attachment which delivers an alternate hot and cold blast; this is vastly superior to the older methods.

The final section is on the *x*-rays, and appears to be well written throughout; the specialist contributing this portion believes in self-preservation, and wisely.

The writer of this book does not loiter on the by-ways, but prefers rather to keep the practical use of the current constantly before the reader.

The illustrations are exceptionally well chosen for the elucidation of the text, and the volume meets the requirements of the student, physician, surgeon and specialist.

It is the best work in English on the subject of electricity with which we are familiar. N. S. Y.

CONTRIBUTIONS TO MEDICAL SCIENCE. By HOWARD T. RICKETTS, 1871 to 1910. Published as a tribute to his memory by his colleagues, under the auspices of the Chicago Pathological Society; pp. 497; 23 illustrations. Chicago: The University of Chicago Press, 1911.

As indicated in the title, the book is essentially a collection of the publications of Dr. Ricketts and of other workers inspired and directed by him. The work of collecting and classifying the numerous papers was carried on by a committee composed of Drs. Ludvig Hektoen, Preston Kyes, E. R. Le Count, George H. Weaver, and

H. Gideon Wells. The various publications are arranged in well-defined groups which follow one another in the same sequence in which Dr. Ricketts, during his life as an investigator, took them up. With the exception of a few papers which were not included in the book because of limitation of space, the studies presented cover the work in cutaneous blastomycosis, immunology, Rocky Mountain spotted fever, and the tabardillo of Mexico. The whole is unified to a certain degree by the insertion, at the beginning of the book, of an address delivered at the University of Chicago, by Dr. Ludvig Hektoen, on the occasion of the memorial services to Dr. Ricketts.

As indicated above, Ricketts' earlier work was in the field of dermatology, and the first studies presented are those on blastomycosis, or as Ricketts, apparently with great propriety, named the condition, oidiomycosis of the skin. Of these papers, the one entitled "Oidiomycosis of the Skin and its Fungi" is a most comprehensive and exhaustive presentation of the subject, and occupies 157 pages in the book. This is followed by several shorter papers on additional cases of the condition and on the biology of the organism by Dr. Ricketts and his colleague Dr. B. F. Davis. A series of papers on more or less abstract points in immunology is followed by the extensive studies in Rocky Mountain spotted fever. The reader following this series of papers can trace step by step the procedures in the field and the work in laboratory and institute which led to the unravelling of the mystery of this disease. The material presented by Dr. Ricketts is admirably collated and summed up in his Carpenter Lecture before the New York Academy of Medicine, included as a part of the series. Appended are several studies on Rocky Mountain spotted fever carried out by associates of Dr. Ricketts—Drs. B. F. Davis, W. F. Peterson, J. J. Moore, M. B. Mayer, and E. R. Le Count. The papers on spotted fever occupy 172 pages, and the book is concluded with the magnificient studies on the typhus fever of Mexico, during which the heroic worker sacrificed his life.

The book is well printed on heavy paper, is neatly bound in cloth, the illustrations are beautifully presented, including the frontispiece portrait, the grouping of the studies is splendid, and all in all the volume is well fitted to be the permanent memorial to a noble investigator, a man of ability and energy, a man of high ideals and "a pure love for search after the truth in his chosen field." "The torch was placed within the grasp of hands fit to carry it forward and during the few short years given him he advanced it farther than we may realize at this moment, because he broke open paths for future progress."

The medical public suffers in that the introductory address by Dr. Hektoen fails to bring the reader into intimate touch with Ricketts, the man, fails to point out those influences of childhood,

youth, and early manhood that make for that love of truth, scientific achievement, and noble character, so well exemplified in Ricketts' life. At a period when Medicine stands in great need of men such as Ricketts the inspiration of insight into the formative period of his life cannot be overestimated. Nevertheless, the address presents at some length the development of Ricketts' work after he took up active investigation, and points out clearly the great strides forward which resulted from his studies. As a eulogy the address is admirable, and its stimulation cannot fail to be far reaching.

The papers presented are too well known and too diversified to permit of criticism, even if good taste permitted it. All the studies show the painstaking thoroughness and attention to detail that mark the great investigator. The studies are rife with suggestion, and must be of great inspiration to all who read them. H. T. K.

THÉRAPEUTIQUE USUELLE DU PRACTICIEN. By ALBRET ROBIN, Professeur de Clinique Thérapeutique à la Faculté de Médecine de Paris, Membre de l'Académie de Médecine. Volume II; pp. 530. Paris: Vigot Frères, 1911.

THIS work is the second volume of an annual series, representing year by year the lectures given at the Beaujon Hospital by Professor Robin. Each year the treatment of a picked group of diseases of various types is lectured upon in great detail in the twenty-six lectures which constitute the course. The present volume is devoted to infectious diseases—typhoid, erysipelas, and rheumatism; metabolic—polyarthritis deformans, gout, and diabetes; respiratory—pneumonia, acute pulmonary edema, pleurisy, and bronchitis; nervous—cerebral softening, cerebral syphilis, and paralysis agitans; skin—prurigo.

The individual topics are fully discussed with the characteristic French fondness for ultimate classification, which, though burdensome, helps one to appreciate the gratifying exactitude of detail.

One cannot help being impressed by the emphasis laid upon certain points which in our literature do not receive much attention. As an example, over twenty pages are devoted to a discussion of the treatment of the albuminuria in diabetes with a division of the albuminuria into three types and a plan of appropriate treatment for each. However, it is in this difference of viewpoint that the value of a foreign work partly lies.

It is difficult to estimate the value of the entire series from a single volume, but it is scarcely probably that any work of this nature will become very much used outside of France. However, for pleasant reading and suggestiveness, it can be heartily recommended.

O. H. P. P.

DIAGNOSIS AND TREATMENT OF DISEASES OF WOMEN. By HARRY STURGEON CROSSEN, Professor of Clinical Gynecology, Washington University. Second Edition; pp. 1025; 744 illustrations. St. Louis: C. V. Mosby Co., 1910.

THE book contains seventeen chapters. The first three are devoted to methods of examination, diagnosis, and treatment. Then follow chapters on diseases of the external genitalia and vagina, lacerations of the pelvic floor and genital fistulæ, displacements and nutritive and inflammatory diseases of the uterus.

Malignant diseases of the uterus and fibroid tumor are considered separately. The diseases of the adnexa are discussed in three chapters: one on pelvic inflammation; one on tumors of the ovary and the parovarium; and one comprising tubal pregnancy, pelvic tuberculosis, and other minor subjects.

Malformations of the genital apparatus and disturbances of function make up Chapters XIII and XIV. Chapter XV describes the operative technique of abdominal section, vaginal section, and conservative surgical procedures.

The after treatment of operative cases is fully related in Chapter XVI, while the last chapter is entitled "Medicolegal Points in Gynecology." In an appendix to the volume, numerous formulæ are given of cathartics, emmenagogues, ointments, powders, etc., used in the practice of gynecology and pelvic surgery.

The author has endeavored to present the diagnosis and treatment of gynecological diseases as they are met in the office or at the bedside by the general practitioner. Particular and detailed attention, therefore, is given to diagnosis and the selection of ope ative or other treatment.

There is no doubt that the author has succeeded in his effort, for the volume is replete with diagnostic points, and the operative and supplemental methods of treatment as given need no explanation.

The book is profusely illustrated by original and borrowed pictures. These serve their purpose admirably. The original illustrations are not uniformly good from the artistic standpoint, and the appearance of familiar illustrations from other text-books is an unhappy feature.

In some places there is too much breaking of the narrative and to much tabulation for easy reading. The volume is a mine of information, creditably presented. It will be particularly valuable to the man who wishes to do gynecological work, but who has not had an opportunity to acquire much clinical experience as hospital interne or dispensary assistant. B. M. A.

KURZGEFASSTE CHIRURGISCHE OPERATIONSLEHRE FÜR STUDIERENDE UND AERZTE. By DR. AD. OBERST, First Assistant in the Surgical Clinic and Privatdocent for Surgery in the University of Freiburg, i. Br. Pp. 198; 232 illustrations. Berlin: S. Karger, 1911.

THIS text-book for a course in operative surgery includes: (1) Incisions of the Soft Parts, their Repair by Suture, and Hemostasis; (2) Ligation of Arteries in Continuity; (3) Amputations; (4) Excisions of Joints; (5) Operations on the Head and Face; (6) On the Neck; (7) On the Thorax, Spine, and Abdominal Walls; (8) On the Abdominal Cavity, and (9) On the Urogenital System.

The illustrations are good, but not sufficiently homogeneous to render the book very attractive; some are too large, some are badly reproduced photographs, some are good pen and ink diagrams, and others are half-tone drawings. Most of the operations described are those generally approved and in use all over the world, but some might as well have been omitted. Among the latter is Macewen's method of puckering up the hernial sac into a pad, with the intention of strengthening the abdominal wall. There is no mention of the inguinal method of operation for femoral hernia, as practised by Ruggi and others, which undoubtedly offers great advantages over the classical approach from below Poupart's ligament, especially when an intestinal resection must be done. Nor is Bunge's method of amputation described, nor methods of amputation for cinematic prosthesis (Vanghetti, Ceci, and others). On the whole, however, a sufficiently full account is given of such typical operations as can readily be done on the cadaver, or as will come within the experience of the general practitioner.

A. P. C. A.

SYPHILIS: ITS DIAGNOSIS AND TREATMENT. By F. J. LAMBKIN, Col. R. A. M. C., London. Pp. 195. New York: Wm. Wood & Co., 1911.

THIS work considers syphilis with special attention to the diagnosis and treatment, based to a large extent on the observation and experience of the author. His position has been unique in its opportunities for the study of this disease, since he has been engaged in the treatment of syphilis in the English army, both in England and in India. Moreover, for the last few years he has been in charge of the chief military hospital for venereal diseases. Syphilis, being very common among soldiers, lends itself, however, most excellently to treatment because of the system in the army enabling treatment and observation to be strictly carried out.

The writer begins his subject with a brief, but interesting historical *resume* then passes to the pathology and clinical course of the

six syphilis periods, followed by an exhaustive contribution on the treatment in its various forms. He gives clearly and succinctly the advantages and disadvantages of each method, and rather favors the intramuscular method of administering mercury. He also writes of the modern treatments by the arylarsonates, "Hata" or "606," and points out the great advantage the Wassermann reaction is to modern physicians, both in diagnosis and as an index of the patient's condition. The subject is well covered in all its phases, practical facts emphasized, and no wasting of space on more or less groundless theories.

The diction is good, the style easy and pleasing, and the arrangement and completeness all that could be desired in a book of this size on a subject like syphilis, upon which so much work has been done. E. L. E.

THE WASSERMANN SERODIAGNOSIS OF SYPHILIS IN ITS APPLICATION TO PSYCHIATRY. By FELIX PLAUT, M.D., Scientific Assistant in the Psychiatric Clinic of the University of Munich. Translated by SMITH ELY JELLIFFE and LOUIS CASA-MAJOR. Pp. 189. New York: Journal of Nervous and Mental Diseases Publishing Company, 1911.

THE monograph of Dr. Felix Plaut starts with a brief, clear-cut history of the experimental work that lead up to the exposition of the Wassermann reaction, and of some of the later investigation into the nature of the phenomena. He compares critically some of the main modifications of the test, concluding that the original Wassermann test with aqueous solution of syphilitic fetus as antigen is the method of choice. In a brief, suggestive, but wholly undetailed chapter, he reviews the technique, emphasizing fully the rationale of the controls.

In the main body of the book, he studies (1) Those cases of syphilis without involvement of the central nervous system, finding in the vast number of cases a positive reaction in the blood serum and in all cases, a negative reaction in the spinal fluid. The strength of the reaction is in no way parallel to the clinical findings or to the cellular content of the spinal fluid. (2) In paresis he finds a strongly positive reaction in the blood and cerebrospinal fluid. The strength of the reaction in the two fluids being generally equal and in more or less complete agreement with the cytological findings. Here again there is no parallelism between the biological tests and the clinical manifestations of the disease. The positive serological results separate paresis from post-traumatic psychosis, alcoholic pseudo-paresis, and from manic depressive states. Its importance is distinct in differentiating between beginning paresis with depression, and little or no demonstrable mental weakness, and in those other

cases, which show typical manic excitement, with at the same time suggestive signs of paralysis. Here the fact that you may be dealing with a nonluetic psychosis in a syphilitic or in a parasyphilitic or in a non-syphilitic individual makes the formula or type of reaction in these cases all important.

These types are: (1) In paresis a strongly positive reaction in the serum and in the cerebrospinal fluid with positive cell count. (2) In cerebrospinal syphilis a positive result in blood serum, very weak or absent reaction in the cerebrospinal fluid, and a positive cell count. (3) In the psychoses attacking a syphilitic with no involvement of his nervous system a positive serum reaction only.

In the etiology of dementias of childhood, Plaut thinks syphilis plays an important role. The reaction acts here exactly as it does in acquired forms.

The book is abundantly illustrated with carefully chosen cases and the painstaking balancing of clinical manifestations, cytological investigations, serological tests, and where possible anatomical studies make the book most valuable and interesting. One cannot but wish that the chapter on technique were fuller and more detailed and that in a few places the clinical facts were more condensed. The book has a poise, balance, and reserve which makes it stimulating and suggestive. E. P. C. W.

A Manual of Surgery. By Francis T. Stewart, M.D., Professor of Clinical Surgery in the Jefferson Medical College, Surgeon to the Germantown Hospital, and Out-patient Surgeon to the Pennsylvania Hospital. Second edition; pp. 682; 553 illustrations. Philadelphia: P. Blackiston's Son & Co., 1911.

The author has afforded his readers an excellent work in this the second edition of his surgery. The book, primarily for the student, also makes an excellent work of reference for the general practitioner; both of whom have in it a manual stripped of verbiage, useless theories, and non-essentials. It is brief, practical, and sets forth in a clear, concise and well-arranged order the essential facts of present-day surgery.

Many little details of treatment and diagnosis, so often neglected by authors as being too commonplace to need description, are clearly and minutely described with especial reference to their practical application by even the beginner, as a student must necessarily be. All unnecessary historical and bibliographical references have been omitted.

Many of the illustrations are original, being made from photographs of actual cases. The text is clearly and admirably arranged with important words in italics or in heavier type, a good plan

for helping the student grasp the relative importance of the subject under discussion. A good, well-arranged index is added.

Of a necessity much that is important in many phases of the subject is omitted because of a desire to be brief. The chapter on bandages and plaster-of-Paris dressings is rather too concise, and could well be treated more fully, taking, if need be, some of the space now allotted to bacteriology, immunity, etc., subjects that a student is taught elsewhere in his course. It is a question of opinion whether gynecology should be treated as a part of general surgery, but the author has deemed it wise to insert a chapter on this subject.

Finally, the book is good enough, brief and concise enough to fill the wants of a busy student who has but little time to cull the important facts from the non-essentials, as he must necessarily do in many works on the subject of surgery. E. L. E.

PLASTER OF PARIS AND HOW TO USE IT. By MARTIN W. WARE, M.D., New York, Adjunct Attending Surgeon, Mt. Sinai Hospital. Second Edition; Pp. 100; 90 illustrations. New York: Surgery Publishing Company, 1911.

THIS work, originally based for its subject matter on ten years' experience with over 5000 dispensary cases of joint diseases and fractures, has justly received its second edition. The book fills a a want for both private and dispensary surgeons.

The use of plaster of Paris is usually taken up in text-books as a minor matter, about which all should be conversant. The author presents the subject in its entirety, taking up, in order, the minutest details, explaining each detail in a clear, practical, and concise manner. He describes the preparation of plaster bandages and how they can be most economically made, a point of some importance, especially in institutions, their care and general points in their application. He takes up practically examples of all cases in which plaster might be used, and describes in detail the technique of each individual dressing, even explaining how best to pad the edges and remove spots of plaster from the floors, linen, hands, etc., a point but seldom mentioned. The advantages of the various dressings of plaster in isolated cases are discussed, and those advocated that have proved the most satisfactory in the author's wide experience.

The work is well written, important points clearly stated, and abundantly illustrated with numerous good cuts, most of which are original. With this book on one's shelf, there is no excuse for improper application of plaster on any part of the body.

E. L. E.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Paroxysmal Tachycardia.—H. E. HERING (*Münch. med. Woch.*, 1911, lviii, 1945) summarizes his clinical and experimental findings in paroxysmal tachycardia as follows: (1) With regard to the origin of cardiac stimuli in paroxysmal tachycardia, it is established that there are both auriculoventricular and pure auricular tachycardias. (2) Whether the auricular paroxysmal tachycardia, like the auriculoventricular variety, is heterotopic, has not been definitely proved, though the weight of probability seems to favor this view. (3) The stimuli causing an heterotopic paroxysmal tachycardia may be primary heterotopic or heterotopic in the sense that they differ qualitatively from native impulses or stimuli (Ursprungsreize), probably the former. (4) In those cases of paroxysmal tachycardia which have previously been considered as nervous the impulses can only be native. (5) That a paroxysmal tachycardia may be entirely nervous in origin is proved by the experiments in which Hering was able to produce an heterotopic auriculoventricular tachycardia of sudden onset and termination through stimulation of the accelerator during vagus tonus. (6) These experiments also lend support to the view that the stimuli causing extra systoles may be primary heterotopic stimuli, a conception which requires further confirmation, but which is adapted to the explanation of those cases of extra systole in man which are often interpreted as neurotic in origin.

Immunity of Spirochetes to Arsenic.—The experience of many workers seems to show that, in the majority of cases, a single dose of salvarsan is insufficient to produce a cure in syphilis. The tendency

at the present time is to give repeated injections of the drug. As it has been shown that other protozoa, namely, trypanosomes, may acquire an immunity to arsenical compounds, it becomes of great practical importance to know whether spirochetes are capable of developing a similar immunity. M. ROTHERMUNDT and J. DALE (*Deutsch. med. Woch.*, 1911, xxxvii, 1790) have undertaken an experimental study of this question in connection with chicken spirillosis. It seemed impracticable to study the Spirocheta pallida itself in experimental animals, because of the long intervals of time required to transfer the infection from one animal to another. Atoxyl and salvarsan were the preparations used. Rothermundt and Dale found that passage of the organisms through twenty chickens within a period of two months, the animals being constantly under arsenical treatment, led to no appreciable immunity to the drug on the part of the spirochetes. They therefore believe that there is little cause to fear the development of arsenic immunity on the part of the Spirocheta pallida in patients subjected to repeated injections of salvarsan.

The Babinski Phenomenon in Uremia.—H. CURSCHMANN (*Münch. med. Woch.*, 1911, lviii, 2054) publishes further observations upon Babinski's plantar reflex as a sign of impending uremia. Illustrative cases are described in some detail. Curschmann's experience with the test leads him to conclude that in nephritics considerable valuable information may be gained by constantly testing for the Babinski phenomenon. In threatened uremia the Babinski reflex may become positive before there is any mental disturbance or before the appearance of the preuremic increase of the tendon reflexes.

Salvarsan in Kala-azar.—A. CHRISTOMANOS (*Deutsch. med. Woch.*, 1911, xxxvii, 1705) has tried salvarsan intravenously in the treatment of kala-azar. He used it in doses of 0.007 to 0.01 grams per kilo. of body weight. There was no discernible effect on the course of the disease and no noticeable decrease in the number of parasites. The staining reactions of the organisms were also unaffected. The drug is therefore probably without value in the treatment of kala-azar.

Adrenalin and Asthma.—H. JANUSCHKE and L. POLLAK (*Arch. f. exp. Path. u. Pharm.*, 1911, lxvi, 205) have made an experimental and clinical study of the effect of adrenalin upon the bronchial musculature. It has been observed previously that adrenalin was useful in the treatment of bronchial asthma, and the present investigation was made to determine the cause of the favorable action. The experiments were performed upon dogs and cats. To produce spasm of the bronchioles, muscarin was employed. Januschke and Pollak found that intravenous injections of adrenalin caused an increase of the respiratory excursions of the lungs. The increase, however, was less noticeable in normal animals than in those suffering from "muscarin asthma." The antagonism observed between muscarin and adrenalin made it clear, furthermore, that bronchial spasm, and not embarrassment of the pulmonary circulation, was the chief factor in the production of muscarin asthma, since it was shown that the spasm was relaxed by adrenalin. Asthma produced by the injection of peptone was also relieved by adrenalin, but

that caused by B-imidazolylethylamin was unaffected. They found, too, that the bronchial dilatation which adrenalin induces was not overcome by ergotoxin. The findings reported are of interest in explaining the action of adrenalin in bronchial asthma. By the use of adrenalin injections Januschke and Pollak say it should be possible to determine to what extent bronchial constriction plays a role in the production of other forms of asthma. They have studied a few cases, and their results make it seem probable that spasm of the bronchioles is an important factor in the asthmatic attacks so often seen in cardiac and renal insufficiencies, as well as in the transient dyspneas of pulmonary emphysema. That one of the causes of transient bronchial spasm is irritation of a bronchial constrictor centre in the medulla from congestion is probable, since clamping of the superior vena cava, the vagi being intact, produced narrowing of the bronchi.

The Immediate Effects of Splenectomy on Hemolytic Jaundice.—F. MICHELI (*Wien. klin. Woch.*, 1911, xxiv, 1269) reports remarkable improvement, in fact, an apparent cure, following splenectomy in a patient with acquired hemolytic jaundice. The patient had been under observation for three years and presented all the clinical, hematological, and biological symptoms of the disease. Various forms of treatment had caused only slight temporary improvement. The icteric hue never disappeared. For three months prior to operation, the highest red count was 2,600,000, the lowest 980,000. Following splenectomy, the urine, which had been rich in urobilin, cleared almost at once, and in a few days the jaundice had entirely disappeared. The liver returned to its normal size. Likewise, the hemoglobin rose from 30 to 65 per cent., the red count from 1,800,000 to 4,000,000. The resistance of the red cells to hypotonic salt solutions, markedly lowered before the operation, now became normal, and at the same time the erythrocytes showing the reticulofilamentous substance on vital staining diminished from 25 to 50 per cent. before splenectomy to the normal proportions. About two months after the operation the patient was apparently perfectly well, and felt well for the first time in years. The spleen was found to be sterile, containing neither bacteria nor protozoa. The injection of fragments of the spleen into the peritoneal cavity of guinea-pigs caused no symptoms of disease within thirty days.

Eosinophilous Cells in the Gastric Contents in Achylia Gastrica.—S. MOACANIN (*Wien. klin. Woch.*, 1911, xxiv, 1335) has been able to find several reports where numerous eosinophile cells have been observed in the wall of the stomach post mortem in cases of carcinoma ventriculi and of achylia gastrica. Such cells, however, have not been noted previously in the gastric juice. In Moacanin's case the patient suffered with achylia gastrica and mucous colitis. Eosinophilic cells were found in the gastric contents, and also in the mucus of the stools. Since the eosinophiles may infiltrate the gastric tissues in the neighborhood of atrophying glands, it is possible that the finding of these cells may be found to be indicative of an atrophic condition of the mucosa.

Secondary Hemorrhage Following the Application of Leeches.—E. WEILL and C. NOURIQUAND (*Presse. Méd.*, No. 87, November, 1911, 881) describe, in addition to primary hemorrhage following leech applications, in certain cases a secondary hemorrhage at the site of application, developing three and one-half to five hours later, often difficult to control, and of considerable severity. They have observed this in 6 of 100 cases, in patients of varying ages and both sexes. A striking feature is that in all cases there existed an enlarged liver, with or without chronic cardiac lesions, albuminuria, and nephritis. They consider the hepatic condition of especial importance, but admit from careful analysis, that the number of leeches applied may play a part in the quickness of development, and severity of the hemorrhage. Similar observations of general hemophilia after leech applications have been made. The phenomenon seems best explained by assuming absorption of hirudine deposited by the leeches at the point of application. This may be very small in amount, but increased by the number of leeches. For experiments show that an infinitesimal quantity of hirudine in the plasma renders it anticoagulant. Weill and Nouriquand have demonstrated this *in vitro* by diluting "hirudinized serum," and testing it with 50 or 100 times its content of blood; or by adding equal amounts of calcium chloride or diphtheria toxin without coagulation. Three cubic centimeters of "hirudinized" plasma, with equal amount of the sediment after centrifugalization were injected into a guinea-pig. Twenty minutes later severe hemorrhage developed at the sites of injection, lasting for an hour and ten minutes. In three other animals similarly treated, wounds bled more freely and for a longer time than control pigs similarly incised. Weill and Nouriquand conclude that under certain conditions hemorrhage may develop after leech applications in consequence of a hemophilia due to hirudine. Investigations have been made showing that hirudine is a nucleoproteid, which they hope to demonstrate in the blood of such patients.

Deviation of Complement by the Serum of Healthy Diphtheria Bacillus Carriers in the Presence of Diphtheria Toxin.—E. CATHOIRE (*Compt. rend. Soc. de biol.*, Paris, 1911, lxxi, 315) shows that individuals are found in whose nasopharynx toxic strains of B. diphtheriæ are growing without the least evidence of injury. Such are usually not convalescent from diphtheria; they are generally not affected by local disinfection. Cathoire has attempted to investigate the mechanism of this immunity by testing the patients' serum against diphtheria toxin on the assumption that the bacilli are pathogenic only when their toxin is able to destroy the natural defence of the organism. The method was by trying the complement-fixation reaction of the serum of such carriers in the presence of diphtheria toxin. The sera of 5 patients were considered, in whom toxic bacilli had been found in greater or less abundance for several months. Cathoire first demonstrated that the strain of toxin used did not deviate in doses of 0.5 c.c. a hemolytic system of 1 c.c. of sheep's corpuscles diluted and sensitized, activated by a sufficient quantity of fresh guinea-pig serum. He obtained sharp deviation of the complement, however, with 0.1 c.c. of toxin in the presence of carriers' serum in doses varying from 0.1 to 0.5 c.c. (the power of its hemolysis being first established).

Control, by serum of uninfected subjects showed the integrity of the complement in 9 of 10 cases. Whether in the one case a natural immunity or one acquired from previous infection was concerned the author cannot state.

Finger Phenomenon: A New Diagnostic Sign of Organic Hemiplegia.—ALFRED GORDON, (*Jour. Amer. Med. Assoc.*, 1911, lviii, 1591). The paucity of diagnostic reflex phenomena in the upper limb is striking. The need of such signs is evident in differentiating certain cerebral lesions from spinal or other changes. Gordon reports the following sign in 8 cases of complete hemiplegia: The patient's forearm is elevated. The observer's thumb is pressed against the pisiform body, especially on its radial side, taking care not to press on the extensor muscles or the dorsal surface of the wrist. The patient's fingers are seen to extend, and sometimes to spread in fan-like form. The extension sometimes involves only the last two fingers; in other cases all five. This phenomenon is not very marked in old hemiplegia with marked contracture. In 6 cases of recent hemiplegia (two to six months) this reflex was prompt. In 2 cases it was only obtained after two or three trials. For control, 15 normal patients, 4 cases of brachial palsy of poliomyelitic origin, and 3 cases of hysterical hemiplegia were tested; the reflex was negative in all. Gordon concludes that between this and Babinski's phenomenon there is an obvious analogy; that further observation in many cases for its constancy is necessary.

Brill's Symptom Complex and Typhus Fever.—G. A. FRIEDMAN (*Arch. Int. Med.*, 1911, viii, 4, 427) considers Brill's original article describing a symptom complex characterized as "an acute infectious disease of unknown origin and pathology; of short incubation period, four to five days; a period of continuous fever, accompanied by intense headache, apathy, and prostration; a profuse and extensive erythematous maculopapular eruption; all of about two weeks' duration, whereupon the fever ceases by crisis or rapid lysis, when all symptoms disappear." Brill believes the complex cannot be considered typhus. Friedman believes that the disease in question is in no way different from numbers of typhus cases observed in countries where typhus is endemic, or from sporadic cases observed in the United States and elsewhere. This he thinks is supported by a review of modern literature on typhus, with especial reference to differentiating it from other diseases by modern methods which older observers (cited by Brill) could not employ. From Friedman's own experience of three severe epidemics of typhus fever in Russia, he considers that the picture of Brill's disease is in no way different from his observations of the less severe authenticated cases of typhus, in course, symptoms, and complications. From a review of the epidemiology of typhus, he believes that in many parts of the world the disease is endemic, and may be present for a long time without leading to an epidemic, and that its mortality has considerably decreased wherever good ventilation, abundance of light, and good hygienic conditions exist. Both clinical and experimental observations suggest that lice transmit typhus. If this be provisionally accepted, it throws additional light on the apparent immunity of Brill's ward patients to infection from neighbors

suffering with his disease. For it is well known that lice require more intimate contact than proximity for migration. He concludes that Brill's symptom complex is identical with moderate and mild typhus, and that, as in the far East a corresponding type is called "Manchurian Typhus," so this should not be spoken of as "a disease of unknown origin," but rather as New York Typhus, thus calling the attention of physicians to the clinical picture concerned, and not connoting something rare and unusual.

Vincent's Angina.—EDWIN H. PLACE (*Boston Med. and Surg. Jour.*, 1911, clxv, 720) briefly reviews the literature concerning both the clinical and bacteriological manifestations of this disease, and then considers its general character in the view of over 80 cases seen by himself. The onset is insidious, symptoms varying from trifling to moderate fever; malaise; sore-throat, rarely severe; foulness of breath, and bad taste in the mouth. Often the subjective symptoms are slight. The lesion may be anywhere on the buccal mucous membrane, usually involving the tonsils, and adjacent posterior pillar of the fauces and edge of the uvula. The gums may be affected, or the nose. Place has not seen a case of skin involvement. The lesion consists of a shallow ulcer with sharp cut edges, filled flush with granular cheesy material, colored white, yellow, or green, and on removal foul. Beneath it is a bleeding irregular surface. There is usually an accompanying cervical adenitis, though if marked, due to a complicating infection. The progress may be rapid, with ulceration and destruction of the tonsil. It is usually slower, tending to recover in days or weeks. In Place's experience (differing from other observers) transmissibility of the disease is not noticeable. He attributes its prevalence in asylums rather to the poor dental and oral hygiene. The lesion differs from diphtheria in being primarily an ulceromembranous process. The presence of marked edema and diffuse redness speaks against Vincent's angina. In any case, cultures should be taken. From syphilis, its lack of infiltration, general glandular enlargement, and its course make differentiation possible. From other mouth ulcerations it differs in smear, culture, course, and history. Place has made a considerable number of smear examinations, finding typical organisms only rarely, and in small numbers. Its relation to noma is interesting. In 7 cases of the latter, typical bacilli and spirochetæ were found. The earliest lesion of noma was invariably indistinguishable from Vincent's angina. That the lesion has a specific etiology is suggested from the numbers of characteristic organisms found in typical lesions, disappearing as healing begins; and from the constancy of the clinical and bacteriological pictures. The organism is a long bacillus (4 to 14 μ long by 0.5 μ thick) with tapering edges, staining best with methyl violet, and usually giving an irregularly vacuolated appearance. It is motile, and strictly anaërobic, requiring media rich in animal albumin. The accompanying spirochetes are 6 to 20 μ long, less than 0.5 μ wide, with wide curves. The relation between bacillus and spirochetes is unsettled. The most satisfactory treatment consists in swabbing the ulcer with 100 to 50 per cent. hydrogen peroxide until clean, and painting daily with 2 per cent. chromic acid. Cure usually occurs rapidly.

SURGERY

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The Pathogenesis of Renal Tuberculosis According to Observations on Two Autopsy Cases.—Heresco and Cealic (*Ann. d. mal. d. org. gén.-urin.*, 1911, ii, 1441) report two cases with autopsies, one patient dying after operation. In both cases one lung and the opposite kidney were involved by the tuberculosis, cavities being present in the affected lungs and kidneys. There were no adhesions between the visceral and diaphragmatic pleuræ, nor was there any involvement of the mediastinal or aortic lymph nodes, macroscopically or microscopically. In the first case there were found bacillary lesions of other organs, kidney, ureter, bladder, lungs, epididymis, and hip-joint. These facts seem to show that the path of propagation is by the blood, rather than by the lymph. Tendeloo has two cases in which autopsies were performed. In the first there were bacillary lesions of the lungs and tracheobronchial lymph nodes; adhesions between the right visceral and diaphragmatic pleuræ; bacillary lesions in the upper end of the right ureter; and a caseous node on the anterior surface of the vena cava. In the second case there was an enlarged and painful tracheobronchial lymph node, adhesions between the base of the right lung, the diaphragm, and the liver. The aortic nodes and those of the right renal vein were enlarged and caseous. From these two autopsies, Brongersma concluded that the primary infection is of the lung or the mediastinal nodes, and from there it is propagated by the lymph paths to the kidneys. The two cases reported by Heresco and Cealic demonstrate the opposite view, that the propagation is hematogenous.

The Cure of Prostatic Obstruction.—Young (*Surg., Gynec., and Obstet.*, 1911, xiii, 269) says that his first operations on the prostate, were by the suprapubic route, by which he has operated on 45 cases with a mortality of about 10 per cent. He has done the Bottini operation in 85 cases, but has abandoned it and is using the perineal route, with which his mortality has been about 3 per cent. During recent years he has operated on about 70 cases, in which neither the suprapubic nor perineal prostatectomy were suitable, by a new method—the urethroscopic median bar excision by means of a special "punch." He has had in all about 700 cases, on which he has done one or the

other operation. That radical removal of a carcinomatous prostate can be done through the perineum is shown by the fact that Young has 2 cases alive and apparently well, 1 after six years, and the other case after one year. Perhaps one of the greatest advantages of the perineal operation, as Young performs it, is that after enucleation of the prostate, there exist two lateral extravesical cavities, which can easily be packed with gauze, thus completely stopping the hemorrhage, cavities which rapidly collapse after removal of the gauze on the following day, and which do not form intravesical pouches of suppuration. Another great advantage is that the patient can be up in a wheel chair within two or three days, with splendid dependent drainage. The absence of any case of death from sepsis and the remarkable freedom from lung complications is shown in a series of 450 cases of conservative perineal prostatectomy.

Anesthetization of the Brachial Plexus.—KULENKAMPFF (*Zentralbl. f. Chir.*, 1911, xxxviii, 1337) says that Hirschel's communication on anesthetization of the brachial plexus has led him to report on his own attempts in this direction. The brachial plexus corresponds approximately to the middle of the clavicle. Here, even in fat people, it lies close under the surface, and its cords lie close together. The area to which the needle must pass, is bounded internally by the easily detected subclavian artery, externally by the clavicle and below by the first rib. The nerves lie between the scalenus anticus and medius, where they are surrounded by loose connective tissue, in which fluid easily infiltrates, so that a small quantity of the anesthetic injection will give an extensive effect. The technique was developed on Kulenkampff himself and in operations on his patients. The patient occupies a sitting position, and the subclavian artery is located by its pulsation, which can often be seen with the head in certain positions. It lies almost always where a continuation of the external jugular vein strikes the clavicle. The point of insertion of the needle is just external to this, close upon the upper edge of the clavicle. A fine hollow needle, about 4 cm. long, is made to penetrate almost to the first rib and to seek one of the nerves, when a paresthesia radiates to the arm, and there are seen signs of motor irritation; but there is no pain, as Kulenkampff observed on himself. If the direction of the needle is correct, this paresthesia develops as soon as the skin, superficial and deep fascia are penetrated. The injection of the fluid should be avoided until the paresthesia occurs in the arm, because it will eliminate the tenderness, and thus render difficult or impossible exact exploration. The needle should be directed somewhat inward, backward and downward, in the direction of the second or third dorsal spine. The plexus is about 3 cm. deep, the first rib a little deeper. If the rib is struck without the plexus being met with, it will be because fear of the subclavian artery has caused the needle to pass too far outward. The needle must then be tried successively farther inward, until the paresthesia is obtained. In adults, 10 c.c. of a 2 per cent. novocain-adrenalin solution, with the usual percentage of the latter drug, should be injected. In children, 5 c.c. will be sufficient. As a rule, in from fifteen to twenty minutes the anesthesia is present and involves the whole arm, except for a triangular area over the deltoid. There is also a severe paresis of the whole arm, and a part of the shoulder muscles. The anesthesia lasts

usually from one-half to two or three hours. The method was tried on 25 cases. In 23 a tourniquet was applied to the upper arm without giving the slightest distress. In 1 the tourniquet was removed at the end of an hour because of pain. In 2 cases it was not necessary, and the anesthesia was complete. In 3 cases a few cubic centimeters of ether were necessary. In 15 cases a total anesthesia with a partial paralysis of the arm was obtained. A sufficient hypesthesia in some parts and a complete anesthesia in others were obtained in 5 cases. In 5 others some regions were anesthetic. In a third of the cases the anesthesia did not extend to the region supplied by the supraclavicular and the intercostohumeral nerves. This can easily be overcome by a circular injection of the arm. The method is applicable to all operations on the arm up to the shoulder-joint.

The Treatment of the Duodenal Stump in the Billroth II Method of Resection of the Pylorus.—SCHWARZ (*Zentralbl. f. Chir.*, 1911, xxxviii, 1402) says that while the Billroth II method of pyloric resection has the unquestionable advantage that the divided ends of the duodenum and stomach are not exposed to the same tension at the line of sutures as in the Billroth I method, it has a disadvantage in the insecurity of the duodenal closure. A fatal termination often results from fistula formation, suppuration, and peritonitis. For this reason Brunner sutured the duodenal stump into the abdominal wall. Steinthal covered it with omentum and a gauze tampon. Kausch regarded this danger so seriously that he gave up entirely the Billroth II method (closure of the gastric and duodenal stumps with a gastro-enterostomy) and preferred the Billroth I method (end-to-end suture of the duodenal and gastric stumps). There is evidently no reliable, primary method of closing the duodenal stump. Schwarz believes that he has a simple method which serves the purpose. The difficulty in closing the duodenum securely lies in the fact that the posterior wall is not completely covered with peritoneum, so the closure by a Lembert suture is impossible or only incompletely so. Schwarz employs the following method: Pylorusward from the clamp grasping the duodenum he introduces a careful, continuous occlusion suture, taking in all of the layers. The clamp is then removed and the edges of the peritoneum brought together behind the duodenum by a continuous, superficial suture for at least 3 cm. The portion of the duodenum involved in the operation is then completely surrounded by peritoneum. Then follows a purse-string suture catching the peritoneum. Before tying this suture, the end of the duodenum with the first line of sutures (for occlusion) is pressed into the duodenum. After tying the purse string there will be a complete closure, and there will be no necessity for the aid of the omentum, for drainage or a tampon.

A New Method of Re-uniting the Divided Ureter.—FORSSEL (*Zentralbl. f. Chir.*, 1911, xxxviii, 1369) says that in the removal of a large retroperitoneal fibromyoma, he divided the left ureter where it lay in a groove in the tumor, and pulled the ureter out of the pelvis with the tumor. As he had no confidence in the methods of treating this condition, he devised one at the time. He concluded to pass the upper divided end into the lower, and in order to be able to remove

a sufficient portion of the mucosa of the lower end for contact with the external surface of the upper end, he divided the lower stump longitudinally about 1 cm. from the end. The mucosa was then removed for about 0.5 cm., which was not difficult, with the proper fixation of the ureter. The renal end was then drawn into the vesical end by means of a mattress suture of catgut, which was introduced through the whole wall a few millimeters from the end of each stump, directly opposite the longitudinal incision, the sutures being tied on the outside of the lower stump. The longitudinal incision was then closed by two catgut sutures, and the transverse margin of the lower stump was sutured to the outer layer of the upper stump. A tampon was placed to prevent urinary extravasation, but it was not necessary and was soon removed. Almost two years later, it was established by ureteral catheterization that the urine came out of the left ureter rhythmically, and that the catheter passed without any signs of resistance at the site of the wound in the ureter. A search of the literature showed that Gubaroff had done a similar operation, but without removal of the mucous membrane. Death of the patient on the thirty-first day had no relation to the operation. A postmortem showed complete restitution of the ureter. Pozzi did an operation in which he tried to bring the connective-tissue surfaces together, but four or five months later a stricture was found in the ureter at the site of the operation. Forssel thinks that this operation is to be preferred to all others, when it can be carried out, because of its simplicity; because it provides immediately at the site of the wound a good hindrance to the escape of urine; it is well suited for a quick and safe adhesion of the apposed ends of the ureter; it makes only a small sacrifice of the length of the ureter; and it does not sacrifice the normal opening of the ureter into the bladder.

A Contribution on the Employment of the Tubular Speculum in Laparotomies.—Nyström (*Zentralbl. f. Chir.*, 1911, xxxviii, 1403) says, in connection with Kuhn's recent contribution on this method in the *Zentralblatt*, that Gärdland, of Stockholm, has been using for two years in cases of peritonitis, a rectal speculum, very similar to the instrument employed by Kuhn, and has been using it in the same manner for obtaining a deep view of the peritoneal cavity through a small incision in the abdominal wall. Nyström has been employing a modification of the usual tubular rectal speculum. The rounded end of the obturator fitting into the speculum is made of glass, and is carried to the bottom of the speculum by a narrow handle, which permits a view through the glass end when it is in position. The usual electric lamp can be employed for light. Through this glass window at the end of the speculum the introduction of the instrument can be controlled. Nyström is more conservative than Kuhn as to the availability of the instrument for a complete examination of the abdominal cavity. Omentum and mesentery can so obstruct the speculum as to make it difficult or impossible to see some parts of the abdomen. In one case with symptoms of peritonitis, which was at first taken to be one of cholecystitis, a small abdominal incision was made along the right costal margin, and the speculum introduced. The upper part of the abdomen could be rather easily examined, but no focus for the

peritonitis could be found, as the peritoneum was everywhere smooth and shining and showed no exudate. Then the speculum was passed to the middle and lower parts of the abdomen, but no exudate could be seen here, nor could the appendix or cecum be seen. Only after enlarging the wound and introducing the finger, was there found an infiltration behind the upper part of the ascending colon. Through an incision at a suitable place a gangrenous appendix with abscess was exposed and extirpated. With more experience, its usefulness will be increased and its limitations become better known. Even without a specially developed technique it is very serviceable. Several weeks before the reading of his paper, Nyström operated on a case of fracture of the pelvis with symptoms of rupture of the bladder, supposed to be on the anterior side. The prevesical space was opened by a median incision above the symphysis, and in the wound was found a considerable infiltration of urine. With the finger there was felt deeply a suspected place of rupture. With a small rectal speculum, without further enlargement of the wound, there was seen a small rupture, and through the speculum a Nélaton catheter was passed into the bladder. In order to exclude an intraperitoneal rupture, an incision was made in the peritoneum close to the bladder, wide enough only to pass the speculum. The posterior wall of the bladder and surrounding parts were examined. In the neighboring intestine and mesentery were found small hematomata, but the bladder wall was smooth and free of peritoneal irritation and exudate.

Concerning the Circular Suture of Vessels, Arteriovenous Anastomosis, and the Transplantation of Vessels.—Yamanoüchi (*Deut. Zeit. f. Chir.*, 1911, cxii, 1) made an experimental study of bloodvessel suture, his observations being based upon 117 operations of various kinds. He says that arteries and veins divided transversely can be reunited very successfully. The healing at the line of sutures takes place by connective tissue, in which a part of the elements of the vessel wall is preserved in the line of union. The failures in circular suture are due to defects in the technique. For the filling in of an arterial defect from resection, a piece of vessel from the same individual is best suited. The transplanted vessel, whether artery or vein, lives permanently. If a vein is employed, it soon withstands the arterial blood pressure, because its wall increases in thickness. The healing at the line of sutures results from new tissue formed from the implanted and original vessel stumps, as well as from the perivascular tissue. The autoplastic implantation of a piece of vein into an artery is to be recommended as a surgical procedure, since the vein, even if it is larger, can be resected, as a rule, without noteworthy disturbances. It is, possible to transplant a piece of vessel into an arterial defect of another individual of the same or another species. The transplanted vessel, however, slowly disappears, and is substituted by the body tissues, so that finally it is surrounded by a connective-tissue tube, which is coated internally by epithelium developed from the ends of the stumps of the body vessel. The healing at the line of sutures takes place merely by growth from the body tissues, while the transplanted vessel remains wholly passive. In practice this method is not suitable, because dangerous complications may result, such as secondary

hemorrhages and aneurysmal formation. Portions of arteries from recently dead animals of the same species may be transplanted successfully. Histologically and practically, the process is the same as in the above. It is also possible to transplant successfully portions of vessels, preserved in Lock's solution, physiological saline solution, or sterile water at a temperature of 0° to 1° C. The preserved vessels before transplantation show no noteworthy histological changes. Whether it lives or not has not yet been established. At any rate, after transplantation, according to the individual differences, it will be slowly resorbed and substituted by the body tissues. Finally, even dead portions of vessel may be transplanted with success. This is an interesting experiment, physiologically, since it shows that the presence of living vessel epithelium is not absolutely necessary to prevent intravascular thrombosis. Circular arteriovenous anastomosis is an operation which is easily carried out. The blood afterward flows peripheralward, while the resistance of the valves disappears. The question whether the blood flows back through the capillaries to the heart or through the anastomosis with the vein, is not yet solved.

Fibro-epithelial Tumors of the Mammary Gland.—GREENOUGH and SIMMONS (*Annals of Surgery*, 1911, liv, 517) say that a comparative study of the fibro-epithelial tumors of the breast shows that their relations one to another are very close, and justifies their being grouped together as in the Warren classification. The essential features of the tumors of the fibrous types is the presence of periductal fibrous tissue in more or less abundance about the gland ducts. This periductal fibrous tissue may vary in cell richness from normal fibrous tissue to myxomatous or sarcomatous tissue. The two types of tumor, however, with this exception, are so much alike that the sarcoma type may be well considered merely a modification of the benign fibroma. The periductal fibroma needs only excision of the tumor to effect a cure. For the periductal myxosarcoma, amputation of the breast is advised, without removal of the muscles or dissection of the axilla; the tumor is only locally malignant. The fibrocystadenoma group includes a few tumors of similar origin to the foregoing, which display, when examined by the microscope, a tendency to epithelial overgrowth. The diagnosis between fibrocystadenoma and periductal fibroma cannot be made with certainty before the removal of the tumor. This tendency to epithelial proliferation is encountered in other diseases of the breast, such as abnormal involution of cystic disease; and is an undoubted source of danger to the patient in adult life. For this reason complete removal of any fibro-epithelial tumor of the breast by early operation is the best treatment to be advised.

On Impacted Fracture Through and Near the Femoral Neck.—COPE (*Annals of Surgery*, 1911, liv, 682) says that impacted fracture of the neck of the femur (within the capsule) is by no means an uncommon occurrence. It results from direct violence applied over the trochanter major, and may permit of considerable voluntary and passive movement of the hip without crepitus. An unimpacted fracture resulting from indirect violence may occasionally be converted into an impacted fracture owing to an immediately subsequent fall upon the

affected hip. The impaction may cause an atypical deformity, even sometimes simulating a dorsal dislocation. Fracture of the base of the neck is always primarily impacted; if the force applied is great, there are always secondary fractures, both horizontal and vertical, through the trochanter region. Persons with impacted fractures of the femoral neck or base of the neck may and often do walk about for some days after the accident. An impacted fracture of the base of the femoral neck may exist without appreciable shortening when the force is not sufficient to cause the trochanter region to be split up by the wedge-like cervix femoris.

THERAPEUTICS

UNDER THE CHARGE OF

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The Action of Iron and Arsenic as Remedies for Chlorosis.—ZWETKOFF (*Zeitschrift f. Exper. Path. und Therap.*, 1911, ix, 393) compares the results obtained by the treatment of chlorosis with iron and arsenic alone with those obtained by treatment with iron and arsenic combined. The conclusions are as follows: The treatment of chlorosis with arsenic in the form of arsenous acid, either given by mouth or subcutaneously, does not result in an increase of the hemoglobin or of the number of red blood cells. The action of arsenic in chlorosis is in direct opposition to its effects in pernicious anemia. In the later disease the arsenic treatment is of the highest value. This difference of action of arsenic in these two diseases of the blood-forming organs is dependent upon some difference in the nature of the two diseases. The treatment of chlorosis with iron in the form of Blaud's pills results in a rapid increase of the hemoglobin and when the blood cells are diminished an increase in their number. This regeneration of the hemoglobin and of the red blood cells is not rapid as measured by the single weeks. The treatment of chlorosis with iron and arsenic combined gives a definitely increased improvement in comparison to the results obtained by the treatment of chlorosis with iron alone. The increase of the hemoglobin occurs more rapidly, and the number of red blood cells shows an increase of two or three times that obtained when iron alone is used. The arsenic is given in the form of arsenous acid, in doses of from 0.002 to 0.003 gram three times a day. These doses are combined with the ordinary doses of iron. Zwetkoff believes that the increased benefits derived from this combination of iron and arsenic is not only a question of the added action of arsenic to iron, but that it is to be explained on the ground that arsenic directly stimulates the bone marrow, that is being coincidently supplied with iron, to increased blood production.

Digitalis.—Mackenzie (*Heart*, 1911, ii, 273), in a long article, reports 43 cases of various cardiac affections treated with digitalis. Each case is presented with a wealth of clinical details regarding, particularly, the effects produced by the administration of digitalis. Mackenzie draws the following conclusions from his detailed study of these cases: The careful analysis of the symptoms of patients to whom digitalis has been administered brings out the fact that individuals react differently to the drug. So far as the heart is concerned, the difference is partly dependent on the nature of the lesion with which the heart is affected. Patients with auricular fibrillation are more readily and more markedly affected than patients with the normal rhythm. Digitalis, in a proportion of patients with normal rhythm, affects the auriculoventricular bundle more particularly, producing partial heart block. It is suggested that the susceptibility of patients with auricular fibrillation may result from the tendency of digitalis to affect the bundle, the change in the auricular condition rendering the bundle more susceptible to the influence of the digitalis. It is possible that in slowing the heart's rate the digitalis acts by stimulating the vagus nerve. Digitalis tends to induce auricular fibrillation. In two cases of tachycardia, arising from an abnormal source, digitalis caused the heart to revert to a normal rhythm, first inducing fibrillation of the auricle. The diuretic effects of digitalis may be produced with no perceptible change in the heart.

Clinical Observations on the Physiological and Therapeutic Action of Large Doses of Radium Emanation.—Von Noorden and Falta (*Med. Klinik*, 1911, vii, 1487) believe that large doses of radium are only indicated in certain forms of acute articular rheumatism in which both large doses and prolonged sittings seem to be most efficient. In all other diseases v. Noorden and Falta advise beginning with small doses and then gradually increasing them. Large doses of radium should be given to nervous patients only with the greatest caution. They believe that radium has a profound effect upon the body metabolism, and cite their findings to support this view. In their opinion treatment by radium emanations is best carried out in institutions, since a strict régime and care as to details of the treatment aid its beneficial effects. It is probable that many of the beneficial effects obtained at certain spas may be explained by the baths containing more or less radium in its natural state.

The Action of Heart Remedies.—La Franca (*Zeit. f. Exper. Path. und Therap.*, 1911, ix, 427) from his own experimental and clinical observations has formulated the therapeutic action of various heart remedies in relation to their effects upon the irritability, conductivity and contractility of the heart muscle. He says that contractility of the cardiac muscle is increased by digitalis, spartein, convallaria and cactus grandiflora. On the other hand, strychnine, caffeine, sodium bromide and sodium iodide have no influence upon this property of the cardiac muscle. The irritability of the heart muscle is lessened by both digitalis and cactus. The irritability and the conductivity are both increased by convallaria, strychnine, caffeine, sodium bromide and sodium iodide.

The Diuretic Action of the Amino-acids.—GLAESSNER (*Therap. Monatshefte*, 1911, xxv, 479) says that glycocoll has a marked diuretic action in cases where there is passive congestion due to hepatic or cardiac disease. This diuretic effect is also observed in many cases of renal disease, but is not nearly so marked. Cases of liver disease with diminished output of urine are most remarkably influenced by the action of the remedy. Better results are obtained with glycocoll in dropsy due to cardiac incompetence if the remedy is combined with cardiac stimulants. The diuresis resulting from the action of glycocoll consists not only of an increase of water excreted, but there is also an increase in the solids of the urine. The specific gravity of the urine is increased, the amount of urea and the chlorides are higher. Glaessner says that glycocoll is an entirely harmless remedy, and it is not unpleasant to take. The usual dose given by the author is 5 grams a day. The only disadvantage of the remedy is that it is more expensive than other diuretics.

The Treatment of Hemoptysis with Digitalis.—LOCKE (*Therapie d. Gegenwart*, 1911, lii, 396) discusses the etiology of hemoptysis and points out that it may result from a number of causes other than tuberculosis. Among the most important of these causes he mentions anemia, arteriosclerosis, bronchial asthma, and acute catarrhal bronchitis. In many of these patients the hemorrhage is due to a local congestion that favors diapedesis. Locke believes that the treatment should aim to reduce this local congestion, and for this purpose he recommends digitalis. He has had good results with this plan of treatment, but emphasizes the fact that an accurate diagnosis of the condition causing the hemorrhage is necessary before the treatment is instituted.

The Effect of the Digestive Secretions upon the Activity of Digitalis and Allied Drugs.—HALE (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1515) relates a series of experiments undertaken to determine the effect of the digestive secretions upon the activity of digitalis preparations and strophanthus. He found that the acid of the gastric secretion invariably causes some diminution in the action of the glucosides of digitalis and strophanthus. He does not believe, however, that an exact determination of the degree of decomposition in practice can be made, for in all probability the rate is somewhat more rapid under actual conditions, owing to the motility of the stomach and the comparatively greater dilution of the glucosides. The rate of deterioration, however, appears to be about the same for the various glucosides, about 25 to 35 per cent. in three hours, so that this fact need not be taken into consideration in therapeutics. The further factor, however, of the action of the decomposition products of these glucosides must be considered, and it is possible that certain of the untoward effects of digitalis medication may be due to them. At any rate, in so far as is possible, it would seem advisable to prevent such decomposition, and it is suggested that this might be done by requiring the official galenical preparations to be neutral, and in practice, by prescribing an alkali along with digitalis. Ignoring the specific irritant action of these bodies on the intestinal tract also, it would seem advisable that the drug should be given

between, rather than at meals, when the gastric acidity is at the maximum, and such a procedure might possibly not cause undue irritation if a large quantity of fluid were taken at the same time.

The Use of Hypodermics of Citrate of Iron in the Secondary Anemia of Tuberculosis.—BULLOCK and PETERS (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1428) recommend highly the subcutaneous injections of citrate of iron for the treatment of secondary anemia of tuberculosis. This remedy has been employed in 256 cases, and it has not failed to improve the blood in a single case. Over 70 per cent. of these patients were in advanced and far advanced classes. The subcutaneous injection of iron citrate is a common practice with Italian physicians, and Bullock and Peters advise the use of the Italian preparations because they are less irritating locally. The dosage employed is 0.05 gram injected daily until the blood examination shows a normal condition. In most cases it required but thirty to forty injections to attain this result.

The Effects of Hypodermic Injection on the Secondary Anemia of Chronic Pulmonary Tuberculosis.—BARLOW and CUNNINGHAM (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1435) used subcutaneous injections of cacodylate of iron, sodium cacodylate and arsacetin for the treatment of secondary anemia in pulmonary tuberculosis. Twenty-eight patients were treated, and the tabulated results are recorded and compared with patients not receiving the treatment. They also give the indications and contraindications for the treatment in detail, and the choice of preparation for the individual case. They believe that the following conclusions regarding the treatment are profitable. The subcutaneous or intramuscular injection of sterile solutions of arsenic or iron, or of the two in organic combination, is entirely practicable in the treatment of the tuberculous in sanatoriums. The effects of such medication are seen chiefly in the changes in the blood and in the body weight. The preparations of iron seem to affect the hemoglobin content more profoundly than it does the number of red blood cells. The preparations of sodium cacodylate and of atoxyl (arsacetin) seem to affect the number of red cells more markedly than the hemoglobin. These solutions are in no sense specifics against the tubercle bacillus, but seem to exert a general tonic or alterative action within the organism. The use of these preparations is entirely safe, and is not attended with danger to the patient, even when continued over a period of many months. Relatively larger doses are borne when given thus than are tolerated when given by the mouth. The dosage is capable of exact control, and the amount of the drug absorbed is known definitely. The body weight is more rapidly and more certainly raised when these preparations are employed than when the unassisted, hygienic, dietetic form of treatment is maintained. There is no demonstrable increased liability to pulmonary hemorrhage accompanying the use of these preparations in pulmonary tuberculosis, even with advanced cases, and in the presence of progressive destruction of the lung.

PEDIATRICS

UNDER THE CHARGE OF

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The Vasoneurotic Symptom Complex in Children.—FRANZ HAMBURGER (*Münch. med. Woch.*, 1911, lviii, 2201) thinks that too little attention has been paid to vasomotor changes in the nuerasthenias of childhood, although in adults it is known that arteriosclerosis and functional changes in the heart are associated with and follow neurasthenia. In nervous children many different symptoms are found, all of which can be traced back to an irritability in the innervation of the circulatory system, and of its chief organ, the heart. The symptoms are subjective, relating to the heart, and objective, relating to the vessels. Under the former are found palpitation, unpleasant sensation in the precordium, such as a "stitch," and a feeling of oppression. Palpitation occurs after physical exertion and to a less degree after psychical disturbances. In marked cases more or less pain and dyspnea may occur, and even symptoms comparable to the angina pectoris of adult life. These symptoms are, however, rare in comparison to palpitation. Objectively there is found a heaving, somewhat diffused apex beat, and slight epigastric pulsation. The boundaries of the heart are normal, or but slightly increased, the sounds are clear. The epigastric pulsation is due to the descending aorta, and not to the right ventricle, in Hamburger's opinion. The sensitiveness of the pulse is shown, on the one hand, by a rapid increase in the rate on sitting up, standing and on slight physical exertion, and on the other hand, by a pulsus irregularis respiratorius, increasing with inspiration and diminishing with expiration. This symptom is most marked in severe cases, but also occurs in normal children. Among the subjective circulatory symptoms are headache, similar in onset to migraine, but involving both sides of the head, usually in the occipital region. Sudden local anemias of the brain cause dizziness and unconsciousness, these symptoms and the headache being due not to a general anemia, as is often supposed, but to changes in the vasomotor system. A tendency to cold hands and feet is another symptom of this class, and also the above-mentioned cardiac pains, due, according to Nothnagel, to an ischemia of the heart muscle. Among the objective circulatory signs are noted flushing or paling on psychical disturbance, coldness of the extremities, dermographia, visible pulsation of the carotids, and increased tension of the arterial walls in the radial and temporal arteries. Many forms of bronchial asthma probably belong to this class. There are, besides, a large number of symptoms occurring in combination, all of which can be traced back to a nervous irritability of the whole circulatory apparatus. This "vasoneurosis" is by far the most prominent and important manifestation of nervousness in later childhood (seven to fourteen years), and occurs also in younger children.

The rigidity of the arterial walls in nervousness is marked in many cases, and generally all children with apparently "thickened" arteries are nervous. Normally, under six years, the pulse only, and not the arterial wall, is felt by the fingers; and not until the tenth year are the arterial walls frequently palpable. Pallor, especially in school children, is often construed to be an anemia, whereas it is arterial contraction due to nervousness; such children commonly have dark rings under the eyes. Marked vasoneurotic symptoms do not usually begin until about the seventh year, when the child begins to attend school. As etiological factors, Hamburger attributes an inherited disposition and certain psychical and physical irritating or stimulating influences, such as fright and joy and autosuggestion on the one hand, and toxins on the other. The prognosis of the vasoneurotic condition is good if the psychical causes can be discovered and avoided, and the child's disposition modified by good hygiene and intelligent mental training.

The Blood Pressure in Diphtheria.—J. D. ROLLESTON (*Brit. Jour. Child. Dis.*, 1911, viii, 28) studied the blood pressure in 179 cases of diphtheria. The systolic pressure as measured by the disappearance of the radial pulse was alone taken into consideration, and the instrument was C. J. Martin's modification of the Riva-Rocci instrument. The pressure was taken daily in each case for from three to eight weeks, depending on the severity of the case. All the cases except 15 were children below the age of fifteen years. The maximum blood pressure of normal children, according to Seiler, who used the Riva-Rocci instrument, is 75 to 80 mm. from two to three years; 79 to 90 mm. from four to five years. Cook and Briggs found slightly higher figures with their modification of the Riva-Rocci, and place them at 75 to 90 mm. up to two years, and 90 to 110 mm. after two years. Of the 179 cases observed by Rolleston, 63, or 35.1 per cent. according to Cook and Brigg's estimate, and 45, or 25.1 per cent. according to Seiler's figures, showed for varying periods a pressure below the normal. The varying degrees of depression bore a direct relation to the severity of the attack, being pronounced in severe and slight in mild cases. In the very severe class, of 22 cases, 18 according to Cook, and 17 according to Seiler, showed from 5 to 45 mm. below normal. The fall in pressure occurred rapidly and steeply, there being at times 10 mm. difference between the morning and evening readings. A difference of the reading of the two wrists indicated a grave prognosis. The severe and the moderate class of cases showed a considerable fall, but less marked than in the very severe class; the severe class showing 25 and 16 cases respectively, with falls of from 3 to 24 mm., and the moderate class 11 and 6 cases respectively, showing a fall of from 1 to 14 mm. The greatest difference registered was in one case, and amounted to 38 mm. The moderate class showed the least fall from normal. The occurrence of comparatively high pressures during the first week is due to febrile disturbance before the toxins had taken effect. The preponderance of the lowest readings in the second week accords with the fact that vasomotor paralysis occurs most frequently during this period. In 2 neurotic sisters, aged seven and nine years respectively, the readings ranged between 130 and 148 mm. Hg for a month. The lowest reading in a case which recovered was 60 mm. in a girl aged

three years. In the great majority of cases normal tension was regained by the end of the seventh week. As a rule, the pulse rate followed the degree of blood pressure. Out of 103 cases in whom comparison was made between the recumbent and the erect position, in 48 the readings were the same, and in 32 the recumbent readings were higher than the erect. In only 23 was the normal relation found. This reversal is liable to occur in convalescence from any acute disease. This indicates that the resumption of muscular work should be gradual in patients showing this phenomenon of effort hypotension. The increase of blood pressure was marked in the laryngeal cases, tracheotomy being followed by a considerable fall in pressure. Early serum rashes caused no increased pressure. Late serum disturbances after the second week showed a raised pressure in 40 per cent. of cases. The onset of albuminuria usually is accompanied by a fall in the blood pressure. This is exactly opposite from its effect in scarlet fever. Any change of blood pressure occurring with early palsies were in a downward direction. During late palsies a fall was most exceptional. The estimation of blood pressure is not indispensable in forming the prognosis in diphtheria, the fatal termination being indicated by the characteristic features before the blood pressure had shown the evidence of depression. Favorable results are often found in severe cases by administration of 10-minim doses of a 1 to 1000 solution of adrenalin every two to four hours.

OBSTETRICS

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Puerperal Infections.—Polak (*Amer. Jour. of Obstet.*, September, 1911) concludes that curetting, douches and examinations during the acute stage of puerperal infection break down the natural barriers and further increase sepsis, the danger increasing as the period of pregnancy advances. In acute sepsis neither the endometrium nor the placental site should be curetted in cases of acute streptococcic infection. The instrumental emptying of the uterus should not be done after eight weeks pregnancy. The best of all methods consists in digital exploration and emptying in these cases. After the uterus is thoroughly emptied the pelvis should be left undisturbed except for posterior drainage, and treatment should be addressed to improving the patient's general condition. If examination shows that the blood stream is sterile, with a leukocytic resistance, the prognosis is favorable. A local exudative focus in a puerperal patient should never be disturbed so long as the patient gains. Should pus form, the collection should be opened by extraperitoneal incision. Pelvic peritonitis, with exudate, often follows endometritis which has been neglected or improperly treated. Thrombophlebitis must be considered as a

conservative process, and care should be taken not to disturb it. In the majority of cases the natural power of resistance of the patient is localized and circumscribed, the infection ultimately destroying it. It is possible for enormous abdominal exudates to disappear without operation, and even when the tubes and ovaries are involved they may recover spontaneously. No operation should be undertaken during the acute stage of infection, and vaccines may be given to advantage in some cases.

Decapsulation of the Kidneys for Eclampsia.—LONGARD (*Monatssch. f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 4) reports 11 cases of eclampsia treated by decapsulation of the kidneys. One died twelve days after operation, the convulsions having ceased and the secretion of urine having become established. The patient died of septic infection. She became maniacal on the third day and tore off the bandages infecting the wound. In the eleventh case the convulsions ceased after operation, and the secretion of urine increased. Death followed on the fifth day from sepsis, and autopsy showed the origin of the infection to be within the uterus. In 1 case operated upon by a colleague, but one kidney was decapsulated. Operation was performed twelve hours after delivery; death followed three hours later. It is possible that this patient's life might have been saved had both kidneys been subjected to decapsulation. In another case, in which operation was performed twelve hours after delivery, hemorrhagic nephritis, followed by complete suppression of urine, caused the patient's death. Here, evidently, operation was performed too late. A comparison of the results of this operation with the series of cases of eclampsia treated by other methods in the same hospital gives an improvement in the results with decapsulation. In the first, 55 per cent. mortality was recorded; in the second, 18.7 per cent. The clinical phenomena in these cases were practically the same. There was found in the bladder a small quantity of highly albuminous and somewhat bloody urine containing casts. After the decapsulation the quantity of urine increased and the albumin grew less, until a normal condition ensued about the fourth day. On inspection, the kidneys were a yellowish white, often with greater or smaller points of hemorrhage, the whole indicating parenchymatous nephritis. In performing the operation ether anesthesia was chosen. The operation should proceed as rapidly as possible, and double decapsulation, with suture of the wound, can be performed in from twenty to twenty-five minutes. Bergmann's incision was employed and the capsule incised the whole length of the kidney, and separated by pressure with gauze sponges down to the hilus; then the kidneys were replaced. In the first two cases the wounds were drained, but not in the remainder.

Section of the Uterus Through the Posterior Cervical Portion.—POLANO (*Zentralbl. f. Gynäk.*, 1911, No. 40) reports 4 cases of section through the uterus in the lower cervical region. In 1 case the pelvis was not contracted, but the patient, in previous pregnancies, had children very large and with very hard crania, requiring perforation. The second patient had a rachitic pelvis and was operated upon by lumbar anesthesia. Pituitrin was given hypodermically to excite

uterine contractions. The third patient had a normal pelvis, but suffered a prolonged and painful labor from premature rupture of the membranes and failure of the child to descend and engage. The fourth patient had a flat, rachitic pelvis with a true conjugate of $7\frac{1}{2}$ cm. The mothers and children in these cases did well.

The Differential Diagnosis of Ectopic Gestation.—VELITZ (*Monatssch. f. Geburts. und Gynäk.*, 1911, Band xxxiv, Heft 4) reviews his experience in 32 cases of ectopic gestation, and draws attention to the difficulties in diagnosis. The presence or absence of hematocele adds much to the difficulty of diagnosis. The practical conclusion in these cases is to consider the patient as one having a malignant growth, or, at least, a tumor requiring removal. A positive diagnosis may only be made by operation, and the conditions present dealt with in accordance with the nature of the case.

Repeated Ectopic Pregnancy.—RICHARD SMITH (*Amer. Jour. of Obstet.*, September, 1911) reports 4 cases of repeated ectopic pregnancy. In 1, upon a second operation, rupture was found with an adherent appendix and adhesions. A similar finding was present in the second case. The other 2 were typical, and all made good recoveries from the second operation. Smith has collected from American observers 1608 cases, in which 58 were subjected to a second operation. In foreign literature he finds the report of 1390 cases, in which 55 were subjected to a second operation. In his correspondence he has found 2 cases in which ectopic pregnancies occurred three times. Normal pregnancy following ectopic pregnancy occurred in his own 33 patients three times. As regards the question of treatment, he concludes that if the woman has had no children, and is young and desirous of having children, in operating for ectopic pregnancy, if the opposite tube is normal and not closed at the extremity, it should not be removed. Where the patient has had children, we should, if possible, obtain her desires upon the matter and leave the tube, unless it is absolutely closed. Where the patient has had children, and requests that both tubes be removed, this request should be carried out.

GYNECOLOGY

UNDER THE CHARGE OF

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Treatment of Injured Ureters.—STOECKEL (*Zeit. f. gyn. Urologie*, 1911, iii, 51) calls attention to the fact that while obstetric injury to the ureters is becoming less frequent, owing to earlier interference in difficult cases, gynecological injuries are increasing greatly in frequency, because of the increase of extensive operations—especially the radical

operation for carcinoma of the uterus—and also due to the fact that many inexperienced operators are now attempting these difficult operations. Stoeckel asserts most emphatically that in all cases, except where a malignant growth is present, it is the fault of the operator if the ureter is injured. It matters not in these cases whether the ureters follow a normal course or are displaced by a tumor, or whether the operation is performed by the abdominal or vaginal route, injury to the ureter is always avoidable if proper precautions are taken. Where a malignant growth is present, however, it is a different story. Here it may be necessary to isolate the ureter for long distances, to dig it out from its carcinomatous bed, to cut through it, or to resect it. The author has found that the ureter can stand simple isolation from the surrounding tissue for a distance of 10 cm. or more without undergoing necrosis. Such ureters may later become compressed by contracting scar tissue around them, but they never become obliterated, or even dangerously stenosed, except by recurrence of a malignant growth. The ureter that must be dug out of an indurated, carcinomatous bed always presents the possibility, however, of becoming secondarily infected, owing to the injury to its walls, this leading to pyelonephritis or to secondary fistula formation. It may also become the seat of a recurrence of the neoplasm, this occurring, Stoeckel believes, much less infrequently than has been assumed. In very bad cases he recommends, therefore, resection of the ureter on the worst side; he does not favor bilateral resection, as bilateral implantation into the bladder is much more difficult and less certain of success than unilateral. While many ureteral fistulæ heal spontaneously, this is often accompanied by a total or partial occlusion of the ureter, with corresponding reduction or elimination of the function of that kidney; moreover, long waiting for a fistula to heal favors ascending infection. The principle of waiting for months should, therefore, be given up in favor of operation within a few weeks at most. The proper method of treatment is resection and implantation of the ureter into the bladder by the abdominal route, if this is possible. Direct closure of a ureteral fistula by suture of the walls should be limited to cases in which the injury involves less than one-third of the circumference of the ureter, as otherwise stenosis is apt to occur. In doing the implantation the fundus of the bladder should be brought well over to the affected side, so as to cause less tension on the sutures. It is important not simply to make a slit in the bladder wall, but to cut out a little circular piece of tissue, as the opening made in the latter way is much less likely to undergo subsequent contraction. To still further prevent this, the bladder mucosa is stitched to the serosa around the entire edge of the opening, so as to prevent the formation of a granulating wound. The ureter is then passed through this opening so that it projects well into the bladder, and is held in place by fine *absorbable* sutures to the bladder wall, the latter being folded back along the ureter for a considerable distance. Stoeckel demands that the merits of all operations for restoring the function of the injured ureter be judged by the lasting physiological results, these being ascertained by cystoscopic examination at least three years after operation. Where pyelitis or pyelonephrosis is already present, of course a nephrectomy should be done at once. Implantation of the ureters into the intestinal tract or onto

the skin surface should be given up, as both these methods lead eventually to infection and nephrectomy. A simple and oftentimes very useful method of treatment where implantation is impossible, owing to the length of the resected portion, is the ligation of the end of the ureter, with consequent elimination of the corresponding kidney. To accomplish this the ureter should be kinked on itself once or twice, as simple ligation may give way.

Direct Suture of Severed Ureter.—Forssell (*Zentralbl. f. Chir.*, 1911, xxxviii, 1369) expresses views somewhat different from those of Stoeckel, and describes the following method, by which he repaired by direct end-to-end anastomosis a ureter which he had accidentally severed. The wall of the vesical stump of the ureter was slit longitudinally for a distance of 1 cm. from its transversely severed end. Its mucosa was then removed for a distance of 0.5 cm. from the severed end, this being accomplished without difficulty after securing fixation of the end of the ureter. The end of the renal portion of the ureter was then drawn *into* the vesical portion by means of a mattress suture of catgut, which passed through all coats of both stumps a couple of millimeters from the free edge of the mucosa. This was placed on the side directly opposite to the longitudinal slit in the vesical stump, and was knotted on the outside of this. The longitudinal slit was then closed by a couple of interrupted catgut sutures, and the transversely cut edge of the lower stump was fastened in a similar manner to the outer surface of the upper. There was no leakage. Cystoscopic examination nearly two years later showed urine being rhythmically expelled from this ureter, and the ureteral catheter passed the point of injury without any evidence of obstruction. Forssell thinks that this method, where it can be carried out, is preferable to vesical implantation, because it is simple, causes no secondary stricture, leaves the vesical orifice of the ureter intact, and does not sacrifice any considerable length of the ureter.

Treatment of Vaginismus.—Funk-Brentano (*La Gynécologie*, 1911, xv, 633) reports having treated most successfully three cases of vaginismus in recently married women by the following method. Under chloroform anesthesia a Champetier de Ribes bag having a diameter of 5 to 6 cm. is introduced into the vagina, and is then slowly and gradually dilated. It must be remembered in doing this that the extensibility of the parts is much less than in pregnant women, and care should be taken to avoid tears of the vaginal walls. When the bag is full it is pulled upon, so that the perineum bulges and the bag protrudes through the orifice. The hymen is thus put on the stretch, and can be very easily excised. Having done this completely, several little incisions 1 to 2 mm. deep are made around the ring where the base of the hymen was attached. The bag is then extracted without using violence, and a larger one, having a diameter of 7 to 8 cm., is introduced and inflated in the same manner. Great care must be taken in extracting this bag, as much time being employed as in delivering the head in labor. The vaginal orifice now presents the appearance as if labor had just been completed. A manual examination should be made to see if there are any tears, and if such are found they must be

sutured. The procedure is concluded by tamponing the vagina with gauze, which is removed the next day. After this injections are made twice daily into the vagina by means of a well greased, smooth, metal, cannula, the size of which is gradually increased, without the patient being aware of this. Funk-Brentano believes that this method is much superior to the use of specula, as all the muscles of the pelvic floor, especially the levator ani, are stretched by the bags.

Small Fibroids as Cause of Dysmenorrhea.—Wilson (*Brit. Med. Jour.*, 1911, No. 2651, p. 996) relates 3 cases of dysmenorrhea in single women, aged about thirty-two years, in which he thinks the presence of small fibroids was the causative factor. In 2 of the cases the uterus was removed; in 1 of these uteri a small interstitial fibroid, about 7 mm. in diameter, was found in the isthmus; in the other, two similar small nodules were found in the same situation. In the third case a vaginal celiotomy was performed, and the presence of an interstitial fibroid about the size of a hazel nut at the level of the isthmus recognized. This was removed by simple enucleation. All the cases were cured of their symptoms. Wilson believes that the menstruating uterus exhibits a certain degree of "polarity," *i. e.*, the body undergoes intermittent contractions, the cervix dilating at the same time. Anything which interferes with these functions, especially the regular and easy dilatation of the internal os, may be expected to cause pain, and nothing is more likely than that a fibroid of even small size situated in the wall at the level of the isthmus may give rise to such interference.

Vaccine Treatment of Pelvic and Allied Infections.—For the past two years Polak (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1738) has used vaccine therapy in almost every case of septic infection occurring in his obstetrical and gynecological services, irrespective of the time at which it was first seen, his experience for this period covering about 225 cases of various sorts of pelvic and allied infections. He considers the phagocytes the chief factors in combating streptococcic, staphylococcic, and gonococcic infections; these are distinctly increased by bacterial vaccines when used early enough. The prognosis is best when the process is local; where a violent bacteriemia has existed for some time vaccines accomplish little. Polak has found that autogenous vaccines from a single strain give unreliable results, and are much inferior to mixed, polyvalent vaccines from reliable laboratories. Following an injection of these the leukocyte count is usually increased and the polynuclear percentage decreased. It is best to start with a relatively small dose, 25,000,000 to 100,000,000 in most cases, counting the blood four hours before and eight hours after the injection, subsequent dosage being regulated according to the effect produced on the leukocyte count by the initial injection. As a result of his experience, Polak concludes that vaccines are of positive value in thrombophlebitis, and in colon bacillus or mixed pyelitis; in 2 cases of suppurative mastitis they also appeared to be of great service. In the various other forms of infection in which he has used them their value has been more or less uncertain, though in many cases they appear to have aided nature in effecting a cure.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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New Hypothesis of the Pathogenesis of Nystagmus.—None of the hypotheses thus far advanced to explain the production of nystagmus is entirely satisfactory. Arlt's view that the subjects affected with nystagmus displace their eyes in order to supplement a lack of clearness of the image by an additional number of such images in series cannot apply to those numerous cases in which the vision is greatly lowered, but which do not become nystagmic, while others become so with normal or almost normal visual acuity. On the other hand, many children with congenital blindness show typical nystagmus. Moreover, it would be a mistake to believe that ocular disturbances are alone capable of producing nystagmus. The latter has been frequently observed after otitic suppuration. SAUVINEAU (*Annal. d'Oculist.*, April, 1910, p. 295) holds that nystagmus is due to disturbances or lesions affecting the supranuclear centre which presides over the lateral associated movements, as proved by the fact that when recent it is habitually accompanied by a latent diplopia, of which the subject is himself ignorant, but which can be brought out by careful testing with a red glass. Ocular lesions determine the nystagmus when favored by fault of development of the innervation centres of lateral associated movements. This explains why the same ocular lesion does not cause nystagmus in all who are affected with that lesion.

Idiopathic Ciliary Neuralgia.—MONCORGÉ (*La Clin. Ophtal.*, May, 1911, p. 190) calls attention to a form of severe pain, generally unilateral, in and about the eye without any objective symptoms; the pain is usually diurnal, increases on palpation, and occurs more frequently in men than in women. The affection seems to be entirely independent of the refraction; it has been found to occur in eyes entirely normal. Moncorgé is disposed to believe that this functional affection is a principal if not the sole cause of the ordinary headache of undefined character.

Amblyopia Exanopsia.—From an exhaustive study of the pathogenesis of amblyopia exanopsia and strabismus, CAILLAUD (*Annal. d'Oculist.*, December, 1910, p. 385) concludes that there exists an amblyopia from non-use; amblyopia without objective lesion is most frequently congenital, though it may be acquired; the age is without influence upon the degrees of impairment; it is found in hypermetropia, myopia, or astigmatism. A nisometropia appears to have great influence upon the production and degree of the amblyopia, high degrees of which

often accompany slight differences in the refraction of the two eyes. Where such differences are great (3 to 8 D), there is usually but little amblyopia. Weakness of the accommodation does not appear to be a factor. *The amblyopia precedes the strabismus; the latter has no influence upon the development of the amblyopia.* The strabismus only becomes fixed in one eye when the visual acuity of the latter is inferior to its congener; if the visual acuity is equal in the two eyes the strabismus will be the alternating variety.

Exophthalmic Goitre.—FEDERN (*Wien. klin. Woch.*, 1910, No. 16, p. 298) maintains that the disease is due to abnormally high blood pressure. Such elevation depends, as a rule, upon disturbance of the functions of the intestines, which disturbance Federn ascribes to partial atony of the bowel. The disease may also occur as a consequence of other disturbances which result in elevation of the blood pressure. Such disturbances may be seated in the genital system, or may be due to worry, mental overexertion, etc., all conditions which generally cause intestinal disturbances. In many cases an acute element also enters which seems to bring about a sudden development of the affection, but which is really to be regarded as simply an aggravation of an already present, but latent, condition, plus the development of additional symptoms.

Intoxication by Atropine in Children.—COLIN (*La Clin. Ophtalmol.*, December 10, 1910, p. 589) has frequently observed evanescent erythema of the face, chest, and abdomen follow instillations of 0.5 to 1 per cent. aqueous solution of atropine in children aged between two and seven years. Prostration or delirium, so frequently noted in adults, was never observed. In some children the erythema regularly followed each instillation. Most of the subjects were affected with phlyctenular ophthalmia, arguing a reduced condition of the system. The phenomena were particularly noted during the inflammatory attacks, much less frequently in intervals of quiescence. These accidents became very infrequent when collyria in oil were substituted for the aqueous; if the latter are employed the lacrymal puncta should be compressed with the finger.

The Behavior of the Ciliary Body to Antibodies.—SALUS (*Graefe's Archiv*, lxxv, 1) shows that complement cannot be demonstrated in normal aqueous humor. Different antibodies do not pass in the same way into the normal aqueous. Agglutinins and antitoxins pass easiest, while the migration of bacteriolysins is more difficult, and hemolysins the most difficult. The aqueous formed immediately after paracentesis is rich in antibodies, although not to the same extent as serum. The normal ciliary body is completely impervious to albuminous precipitates, but after paracentesis, such precipitates appear in the aqueous; they even appear to occur there with special rapidity. The absolute retention of the precipitates can hardly depend upon special properties of the same; it must be assumed that a certain filtration faculty is possessed by the transuding organ—the capillary endothelium or epithelium of the ciliary body. If the experiment is properly arranged, the precipitation can be followed in the anterior chamber as in a

test-tube. When paracentesis is practised upon an animal which has been treated with human serum, the newly formed aqueous shows distinct flocculent cloudiness. Hemolysins can likewise be shown by the red stain of the aqueous humor. This phenomenon comes out with special distinctness after paracentesis of the anterior chamber.

Ophthalmic Notes in Madagascar.—CRENN, Surgeon-Major in the French Colonial Army (*La Clin. Ophtalmol.*, October 10, 1910, p. 547), from an experience of ten years in medical posts in Madagascar, finds that although that country is affected with paludism in its most severe forms, the ocular affections of malaria are very rare. The lesions observed seem to depend upon the resulting anemia or toxemia. Trachoma is not present, and glaucoma extremely rare; he has only observed a single case. The natives are all hyperopes or emmetropes. Myopia was not found except in a few young school children. He never observed detachment of the retina. The ocular manifestations of acquired syphilis are less grave than in Europe, due, no doubt, to the absence of alcohol, tobacco, and perhaps, myopia.

Treatment of Incipient Senile Cataract with Instillations of Salts of Iodine into the Eye.—KATZ (*Klin. ther. Woch.*, 1910, pp. 36 and 37), in the course of eleven years, has treated more than 60 cases of incipient senile cataract with instillations of sodium iodide. He begins with a 5 per cent. solution, which is progressively reduced to 1 per cent. if the slightest irritation of the conjunctiva occurs. The collyrium was employed at bedtime and from one-half to one hour before rising in the morning. The influence of the instillations upon the course of the opacity is asserted to be marked. In a decided series of cases the treatment inhibited the development of the cataract with the consequent decrease of the visual acuity, or even caused a clearing up to a certain extent of opacities already present.

Retinal Hemorrhage.—ROGERS (*Jour. Amer. Med. Assoc.*, July 8, 1911, p. 99) has made a study of this condition based upon 187 personal cases, omitting specific retinitis, he has classified them as retinal apoplexy, and under five varieties of retinitis, namely, simple hemorrhagic, albuminuric, diabetic, and chorioretinitis. His conclusions are that three-quarters of all cases of hemorrhagic retinitis either terminate fatally within a few years or the subjects suffer marked impairment of health. The prognosis as to life in albuminuric retinitis is better as the patient is older. Any form of hemorrhagic retinitis is suggestive of either present or future disease of either the nervous or circulatory system.

Subhyaloid and Vitreous Hemorrhages.—WOODS (*Jour. Amer. Med. Assoc.*, July 29, 1911, p. 375) concludes that in persons, aged over fifty years, with such hemorrhages, the sign of arteriosclerosis are usually present, or, if not, the hemorrhage itself is evidence. In young subjects there is probably some infection or disease capable of producing vascular changes. When no cause can be found it is nevertheless usually of a serious nature, such as tuberculosis, nephritis, or defective metabolism.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Frambesia, Syphilis, and Salvarsan.—RICHARD D. STRONG communicated to the *Journal of Experimental Medicine* (April 1, 1911) a statement of the great success he has met with in 25 cases of yaws, treated by salvarsan. The usual adult dose, given in the usual way, has produced in yaws the results which we are accustomed to see in syphilis, and has produced them with the same degree of promptitude. It will be remembered that public opinion, which of late rather inclined to the view that yaws and syphilis were identical, has now once more come to consider them as different. Yaws is thought to be due to the *treponema pertenuis*, and the inoculation of both diseases into monkeys is very suggestive as indicating their disparity. It will be remembered by everyone who has been interested in the subject that no previous treatment of yaws has been in any sense satisfactory.

Distempter in Dogs.—Although, fortunately, distemper of dogs is not communicable to the human race, yet the disease is widely known and of such household interest that it is interesting to see that FERRY (*Journal of Infectious Diseases*, June 15, 1911, vol. viii, No. 4) has been able to verify his statement made last year that the disease is due to the bacillus which he then named *bronchicanis*. His observations indicate that early in the disease Bacillus bronchicanis can be isolated in pure culture in all cases. If the investigator waits until the discharge from the respiratory tract makes its appearance, the cultivation of the organism is much more difficult by reason of the secondary organisms which are present. In a fair percentage of cases it was found in the blood, and Ferry was unable to isolate it during life, in the very earliest stages of the disease by use of the bronchoscope. Artificial inoculation with pure cultures has produced the typical disease, and from these cases again the organism has been isolated in pure culture. Further, the serum of dogs suffering with distemper gives positive agglutination with the organism, while the controls have been constantly negative. Ferry is to be congratulated upon a well-rounded and convincing piece of work.

Experimental Typhoid Fever.—METCHNIKOFF and BESREDKA (*Annales de l'Institute Pasteur*, March, 1911) detailed the experiments by which they have successfully inoculated anthropoid apes with the bacillus of Eberth. Considering the difficulties that have previously surrounded experimentation in the lower animals, they were led to ask themselves if the bacillus typhosus was the real cause of the dis-

ease, or whether, as in the case of the bacillus of hog cholera, the scientific world had not been considering the secondary organism as primary and overlooking some minute organism which might prove to be the real cause. Instead of using pure cultures, they began with feces from a typhoid patient, with the result that the young chimpanzee used developed a satisfactory attack of typhoid fever. Further, the fecal typhoid material was filtered, the filtrate given by the intestinal tract, and the rest injected under the skin. This was repeatedly unsuccessful. Not only was it impossible to infect in this way, but it was impossible to protect. Fifteen experiments out of sixteen, using pure cultures of human typhoid or mixed cultures of human and simian typhoid, were successful. The blood of the infected animals in every case developed rapidly agglutinative powers. Experimental typhoid in chimpanzees bears to the ordinary typhoid fever of adults much the same relation as does that of children. There is less prostration, less weakness, less anorexia and apparently no rose spots. The older the ape the more his disease resembles that with which we are familiar. In the three fatal cases that occurred in the series, autopsy showed marked enterocolitis, with great swelling of the Peyer's patches, but never ulceration. Numerous attempts with the infected material of the higher apes proved negative in the production of the disease in monkeys and in other laboratory animals. Metchnikoff and Besredka conclude that experimental typhoid in animals can be produced only in the higher apes and only by way of the intestinal tract. Their positive results were obtained by pure culture of the bacillus of Eberth, and they conclude that there exists no soluble virus to play a subsidiary or primary role in the infection. Vaccination which has proved sufficient to protect laboratory animals against peritoneal infection by Bacillus typhosus is powerless to prevent the typhoid fever of apes, which appears to be the real disease with which we are familiar.

Bone Lesions in Infective Diseases.—Josef Koch (*Zeit. f. Hyg. u. Infekt.*, Band lxix, Heft, 3, 1911), who has been a strong advocate of the infective nature of rickets, brings forward further experimental work in support of that contention. In various kinds of experimental animals he has examined the localization of the injected bacteria in the bony structures. In 20 anthrax-infected animals great, sometimes enormous, masses of bacilli were found in the epiphyseal marrow, especially in the primary medullary spaces of the line of ossification, notably in close association with the vascular loops. Pneumococci appeared to frequent, in addition, the areas of endochondral ossification, and streptococci the perichondrium and periosteum. The great destruction of bacteria that goes on in the medulla is evidenced by the pigment seen in the endothelial cells, and the bacteria found at death constitute only a fraction of the bacteria that have existed there during the course of the infection. The histological changes which are evident as a result of the infection are very marked, both in compact and spongy bone. The spongy bone may be destroyed and the absorption of compact bone greatly hastened. In the general infections, although the heart blood may prove sterile, the juice of the epiphyseal medulla is by no means so, and frequently shows the presence of bacteria. Even in the acute infections of children, such as measles and whooping cough,

the same thing is noted, thanks partly to the osteochondral boundaries in children being a site of predilection for infection. It is true that the pathogenic bacteria, after a time of increase, may be destroyed by specific antibodies, but this short time may be long enough to institute changes in the epiphyses; and the histological changes seen in rachitic bones are oftentimes of a regenerative kind. In 2 cases of florid rickets, with a fatal outcome, Koch found in the femoral epiphyses large numbers of bacteria, and he thinks that the cause of rickets is not to be sought in indefinite *noxæ*, but in bacteria.

Co-incident Abnormality of Numerous Organs of Internal Secretion.—F. HARBITZ (*Zentralbl. f. Allg. Path. u. Path. Anat.*, Band xxii, No. 18, September 30, 1911) reports a case that is very suggestive in its bearing upon the relation that exists among the glands of internal secretion. Autopsy was performed upon a man, aged forty-three years, who had acromegaly which had evidently arisen from hyperplasia of the hypophysis. There was seen hyperplasia of the tissues of the hands, feet, and face, and of many internal organs, especially of the right side of the tongue, larynx, and trachea, of the hypophysis, liver, spleen, right kidney, heart, thyroid, and pancreas—in short, splanchnomegaly. Further, there was hemiatrophy of the left side of the face, of the larynx, and of the trachea, which Harbitz does not feel competent to explain; but in the absence of a discoverable lesion of the trigeminal nerve, of any muscular lesion, and of syringomyelia, he believes that these atrophies must depend upon a lack in the *anlagen* of the organs concerned, especially since the left kidney was similarly affected. More than a coincidence is the fact that not only the hyphophysis and the thyroid were enlarged, but the pancreas and other organs of internal secretion. Harbitz recalls the effect of the hypophyseal secretion on structural growth in general, and the repression of acromegaly after removal of tumors of the organ, as evidenced by Hochenegg, Cushing, etc., as well as the linking that seems to exist between the hypophysis and thyroid on the one hand, and obesity and the failure in genital functions on the other, or again the concurrence of the two last, which Frölich united in the title of *dystrophia adiposa genitalis*. Damage to the glial portion of the hypophysis appears to cause these genital hypoplasias. Harbitz seems to have brought forward another of these interesting cases that appear to show that the glands of internal secretion are intimately associated, and that there is a "polyglandular syndrome," often caused by "pluriglandular insufficiency," but sometimes by what appears to be rather "oversufficiency" of the same structures. Some interesting certainties are arising in this field of unproved suppositions.

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